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HUMAN BRUCELLOSIS IN VICTORIA.

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HUMAN BRUCELLOSIS has been a notifiable disease in Victoria since 1937, although up till the end of 1951 it was listed as "undulant fever"; this term was introduced by Hughes (1897) to designate the *Brucella melitensis* infection then rampant in Malta, but its usage has since been widened to include infections with *Br. abortus* and *Br. suis* as well. However, since the clinical picture is extremely variable and is not always characterized by an undulating pyrexia, the term Brucella infection, or brucellosis, is preferable.

In the first case reported in Australia (Dixson, 1908) the patient almost certainly acquired his infection in Malta, and thus may represent the only case of *melitensis* infection on record. In 1930 Penfold and Butler reported two further cases of brucellosis, one of which represents the first from Victoria; one of these, at least, appears from the cultural data to have been an *abortus* infection, since on first isolation the organism grew only in an atmosphere containing added carbon dioxide.

Figures published in the Victorian Health Bulletin show that since 1937, the first year of official notification of brucellosis, the number of cases reported has risen steadily, if somewhat irregularly, from one to about twenty a year (Figure I). From these figures it might appear that here is a new disease which has been gradually spreading through the community, but in actual fact it is likely that the increase is apparent rather than real, for in Victoria, as in other parts of the world, more cases are being recognized. According to Kaplan (1950), "Brucellosis might be compared to an ice-berg since only its peak is visible to a casual observer". It is the aim of this paper to exhort the observer to be less casual, for in man brucellosis is found only when it is consciously and conscientiously sought.

Natural History.

The three species of Brucella are primarily parasites of certain animals which man has domesticated; *Br. abortus* has a special affinity for cattle, *melitensis* for goats and sheep, and *suis* for pigs, though each of them may, under certain circumstances, wander beyond its customary host range. Human brucellosis almost always represents a spill-over of the infection from an animal reservoir to man, man-to-man spread being correspondingly rare. It appears that the invasiveness of the three strains for man varies considerably, *melitensis* being so highly infective that a number of competent and careful bacteriologists have been infected in the laboratory while manipulating cultures, whereas on the other hand, the drinking of milk infected with *Br. abortus* produces infection but rarely (Clapp, 1953); "it is generally considered that *Br. suis* is more

pathogenic to man than *Br. abortus*" (Sutherland, 1950), so the porcine species may occupy an intermediate position in its tendency to invade man.

In the host of election each strain, according to Sutherland (1950), shows certain pathological characteristics which affect the epidemiology of brucellosis in man. In cattle *Br. abortus* is usually confined to the reproductive and mammary organs; if infected during pregnancy, a cow will often abort, and the ensuing uterine discharge, as well as the fœtus, contains enormous numbers of live organisms. The milk is also likely to be infected. Mammary infection persists, and the uterine infection later becomes chronic, yet the animal may subsequently conceive again; if so, a live calf may be born, though heavy uterine and mammary excretion of living organisms continues. When an infected cow is mated, the bull may acquire a venereal infection, which can then be passed on to other members of his harem. The important point is that in cattle, *Br. abortus* tends to be localized in the reproductive and mammary organs, discharges from which may contain large numbers of viable organisms; these may persist as contaminants of buildings, or even of pastures, where cows are kept.

In swine, on the other hand, *Br. suis* not infrequently spreads beyond the reproductive organs to invade the joints, the bone marrow and the lymphadenoid tissues, and

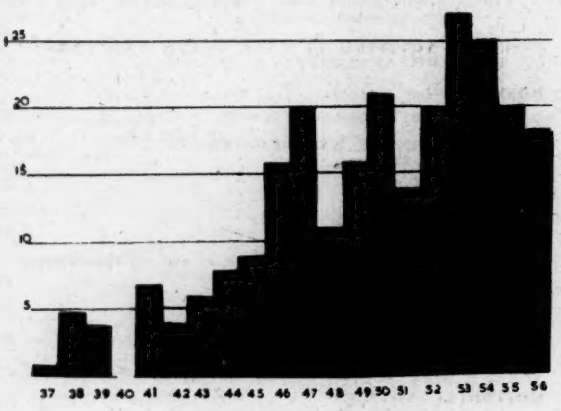

FIGURE I.
Annual notifications of brucellosis in Victoria, 1937-1956.

is often excreted in the urine. It is thus more likely to lurk in foci throughout the dressed carcass.

In man the pathological behaviour of the three species is by no means clear-cut, and the clinical picture resulting from infection is very variable. It has already been mentioned that *Br. melitensis* is the most highly invasive for man, and the classical work of Zammit and others in Malta, described in the report to the Mediterranean Fever Commission in 1905-1907, showed that invasion of man by this species commonly results from drinking infected milk. Conversely, the alimentary route of infection seems not to be the common one in human *abortus* infection; here the portal of entry may be through the skin, damaged or normal, the conjunctiva, and perhaps even the respiratory tract in dust particles, for the organism apparently persists in dust and soil for some time. Just what happens next to the invading organisms of any species we do not know, but there is probably dissemination by the blood-stream at an early stage, followed by localization in phagocytes of the reticulo-endothelial system in almost any organ of the body. Secondary showers of bacteria into the blood may occur, perhaps repeatedly, and focal granulomatous lesions, or frank suppuration, are to be found occasionally in bones, glands, lymph nodes and other organs.

Br. abortus infection in cattle, manifest as contagious abortion, is widespread throughout Victoria and, indeed, in other States of Australia (Seddon, 1948), and porcine disease due to *Br. suis* has been reported from Victoria, New South Wales and Queensland (Sutherland, 1950). There is no record of animal or human infection with bacteriologically confirmed *melitensis* infection, but it is at least possible that the case reported in 1908 by Dixson, apparently acquired in Malta, was due to this species. Because brucellosis is such a chronic disease, the danger of human introduction of *Br. melitensis* from abroad is by no means negligible, and should it percolate back into its natural caprine or bovine host, it could conceivably become truly endemic in Australia.

Clinical Features.

The protean symptoms and signs may be referred either to general toxæmic effects or to focal lesions. In a series of 1233 cases Dalrymple-Champneys (1954) lists the following in order of incidence as the commonest of over 230 symptoms and signs, in addition to pyrexia which is often irregular, remittent or undulant: sweating, weakness, malaise, headache, anorexia, aches and pains, constipation, rigors, splenomegaly, cough, sore throat, arthritis or arthralgia, rash, epistaxis, abdominal pain, visual disturbance, diarrhœa, vomiting, hepatomegaly, depression, adenopathy, insomnia, nausea and loss of weight. To these can be added uveitis, meningismus, encephalitis, suppurative parotitis, endocarditis, jaundice, orchitis, epididymitis and many others. In fact almost any collection of symptoms, even those which are commonly classed as neurotic, can result from Brucella infection; so the condition should never be forgotten in differential diagnosis.

Laboratory Aids to Diagnosis.

Culture.

Unfortunately unequivocal proof of the presence of brucellosis is hard to come by, especially in *abortus* infection, since it can be achieved only by isolating the organism from the patient. Blood-stream invasion seems to be evanescent, for blood culture, even if repeatedly attempted, is successful only in a small proportion of cases. The best time to attempt it is probably when the temperature is rising or during a rigor. Culture of bone marrow, of lymph gland, spleen or liver biopsy, or of urine, fæces, sputum or pus may sometimes yield the organism.

Cultures should be made on a suitable citrated medium, such as one containing tryptose of trypticase-soy, "Albimi" or liver extract, and the method of Castaneda (1955) combining a fluid with a solid agar medium is probably the best. Incubation at 37° C. in an atmosphere containing 10% of carbon dioxide is essential, since *Br. abortus* is dependent on carbon dioxide at first isolation. Cultures should not be discarded as negative in less than three weeks.

Serological Tests.

The demonstration of agglutinins in the serum of a patient suspected of having brucellosis is the most useful method of confirming the diagnosis, but the evidence is no more than circumstantial unless a rising titre can be detected early in the disease. Owing to the insidious nature of the onset, the opportunity for doing this is frequently missed, and the issue may be confused still further by the fact that the level of serum agglutinins may fluctuate considerably during the course of this chronic infection.

Two types of agglutinins, termed for convenience "complete" and "incomplete", may be found in the serum: the first is measured by the direct agglutination test against a standard suspension of a number of smooth strains of Brucella; the second is measured by a modification of Coombs's technique (Coombs *et alii*, 1945) using an anti-human globulin rabbit serum (Wilson and Merrifield, 1951). In some cases at least, the incomplete antibody appears first; and in something like 70% of positive cases, it reaches a higher titre. No constant relation of direct to indirect titre with the stage or activity of the infection is apparent. It is well-known that a prozone not uncommonly occurs in the direct Brucella agglutination test, and it has been found that this phenomenon is eliminated by the antiglobulin test. It seems likely, therefore, that the prozone may be related to the preponderant action of incomplete antibody.

As in any serological test, it is not possible to lay down a "diagnostic titre", but for working purposes a titre of 1:80 with the direct or indirect (antiglobulin) test (against a standard suspension) in a patient with suspicious clinical findings may be regarded as valuable evidence in support of the diagnosis.

In addition to the agglutination test, other serological reactions which have been used to measure serum antibodies include Castaneda's spot test and surface fixation test, and complement fixation, opsonocytophagic and precipitin reactions, but they are not widely used in routine diagnostic work.

Skin Tests.

Skin tests using intradermal injections of brucellin (a diluted culture filtrate) and brucellergin (a purified protein extract) have been used to show the presence of a tuberculin-type of sensitivity. These tests are not quantitative, and they may vitiate the quantitative use of serological tests, since they often cause a rise in the level of serum antibodies. A further shortcoming is that positive reactors may suffer a severe local and general reaction (Stevenson, Ferris and Lewis, 1954). These workers found that the brucellergin test was no more specific than the antiglobulin test; so because of its aforementioned disadvantages it is not advocated.

The positive diagnosis of brucellosis, except in the small number of cases in which a positive culture is obtained, is therefore not categorical; it rests on the history, symptoms and signs elicited from the patient *plus* the serological evidence. Although a medical practitioner is theoretically obliged by law to report every case, some diagnostic doubt often remains, and notification may not be made.

Present Investigation.

Since 1947 the Public Health Laboratory in the University of Melbourne has provided a free diagnostic service in public health bacteriology to all medical practitioners in Victoria, and since that time more and more practitioners throughout the State have availed themselves of it. Study of the records reveals a steady increase in requests for the Brucella agglutination test, particularly over the past six years. The number of tests carried out is as follows: 1949, 182; 1950, 182; 1951, 387; 1952, 575; 1953, 553; 1954, 606; 1955, 761; 1956, 819. These figures include a number of tests which were not actually asked for by the medical attendant, but which, on the clinical data supplied, seemed to be indicated. For instance, sera from all cases of uveitis submitted for Wassermann and Kahn reactions are examined for Brucella agglutinins, and in this way a number of cases of uveitis almost certainly due to brucellosis have been found (Lidgett and Wilson, 1955).

In the three years 1954 to 1956, if we judge from the clinical data supplied with sera which gave positive agglutination reactions at 1:80 or over, 121 cases of probable brucellosis have been collected in this laboratory. This number may be compared with 63 cases officially notified.

Epidemiology.

The official notification figures, published by States in THE MEDICAL JOURNAL OF AUSTRALIA, are divided into cases in the capital city and in the rest of each State. They are shown for the years 1954 to 1956 in Table I.

From Table I it is evident that the number of reported cases per million of populaton is highest in Victoria, and that generally there are more cases in the rest of the State than in each metropolis. This latter fact is clearly brought out in the figures from 1937 onwards for Victoria (Figure II), (*Health Bulletin*, 1956), where more than three-fifths of the population reside in the metropolitan area. Our own figures bring out even more clearly the fact that brucellosis is a disease of higher incidence outside the metropolitan area, for only 26 of 121 persons affected lived in the metropolitan area.

Sex.

As in reports of other observers, including Derrick and Brown (1950), there is a marked preponderance of males over females in the present series. This sex difference is less obvious in children than among adults, though the number of juvenile cases is too small to be significant (Table II).

Occupation.

Of the 121 patients in the series, 63 were farmers (and of these 36 were dairy farmers), seven were meat workers, five were veterinarians, one was a stock agent and one was a milkman, giving a total of 77 in occupations in which handling of cattle or their products was involved. The occupations are set out in Table III.

TABLE I.

Brucellosis Notifications by States.[1]
(Metropolitan cases in parentheses.)

State.	Year Made Notifiable.	Cases of Brucellosis. 1954.	1955.	1956.	Total.	Annual Rate (Per Million).
New South Wales	1937	8 (4)	5 (1)	11 (4)	24 (9)	2·3
Victoria	1937	27 (13)	15 (8)	18 (8)	60 (29)	8·0
Queensland ..	1937	5 (1)	4	11 (2)	20 (3)	5·1
South Australia ..	1954	1	3 (2)	3	7 (2)	2·8
Western Australia	1937	8 (1)	1 (1)	3 (1)	12 (3)	6·1
Tasmania ..	1955	1	1	1	3	3·3
Australian Capital Territory ..	1954	0	0	0	0	—
Australia ..	—	50	29	47	126	4·7

[1] From THE MEDICAL JOURNAL OF AUSTRALIA.

It is quite possible that some of those with occupations classed as "Others" may have handled cows in an amateur capacity.

Geographical Distribution.

Of the 121 cases collected in the three years 1954 to 1956, those in patients who lived outside the metropolitan area are plotted on the map in Figure III.

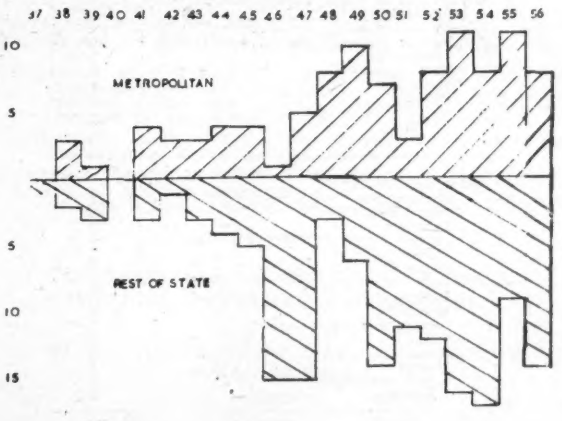

FIGURE II.

Annual notifications of brucellosis in Victoria, 1937-1956, in the metropolitan area and the rest of the State.

Scrutiny reveals a number of districts where cases are concentrated — for instance, around Lilydale, Maffra, Rochester and Numurkah, and lesser groups elsewhere. It is in these areas that brucellosis-minded doctors practise, and from them come many of the requests for Brucella agglutination tests. In the district most productive of cases around Lilydale there is a striking evolution in respect of time (1954, 1 case; 1955, 3 cases; 1956, 6 cases), reflecting a growing interest in the disease among the local practitioners.

The map shown in Figure IV indicates the density of dairy cattle population in Victoria, for comparison with the distribution of our brucellosis cases in man. Whereas these cases are seen to occur in dairying areas, the correspondence is by no means complete, since many milk-producing areas appear to be devoid of human brucellosis.

TABLE II.

Cases of Brucellosis Grouped According to Sex of Patient.

Age (Years).	Sex.		Total.
	Male.	Female.	
Unspecified	5	1	6
0 to 4	2	1	3
5 to 9	1	1	2
10 to 14	2	1	3
15 to 19	2	2	4
20 to 29	22	3	25
30 to 39	34	6	40
40 to 49	26	4	30
50 to 59	3	—	3
60 and over ..	4	1	5
Total ..	101	20	121

Now, according to information kindly supplied by the Department of Agriculture, contagious abortion Brucella is widely distributed in the dairy cattle throughout the State, and it seems probable that the failure to discover cases of human brucellosis in areas shaded in the map (Figure V) is due to failure to look for them rather than to their actual non-existence.

TABLE III.

Occupation.	Number of Cases.
Occupations in which frequent contact with cattle likely:	
Dairy farmer	36
Farmer	27
Veterinarian	5
Meat worker	7
Stock agent	1
Milkman	1
Total	77
Other occupations:	
Home duties	11
School child	8
Labourer	5
Clerical	5
Student	2
Engineer	2
Cook	1
Plumber	1
Bricklayer	1
Cartage contractor	1
Tailor	1
Nurse	1
Dentist	1
Lighthouse-keeper	1
Unspecified	3
Total	44

Discussion.

From the sex, age and occupational incidence it is clear that intimate handling of infected cattle is a more important means of human infection with Brucella in Victoria than drinking infected milk, since otherwise more cases would occur in children and fewer in adult males. There is, however, no denying that milk-borne infection can occur, and that it is the probable explanation for most of the juvenile cases as well as some of those in adults in the metropolitan area who, on occasions, drink unpasteurised milk. The fact that apparently normal cows may excrete the organism in their milk constitutes a strong argument for universal pasteurization.

At least one case, in a veterinary surgeon, was almost certainly due to accidental inoculation with "strain 19", an attenuated live vaccine widely used to inoculate young heifers. The pathogenicity of this strain for man has already been reported by Spink and Thompson (1953) and others when inoculated accidentally into the skin or the conjunctival sac.

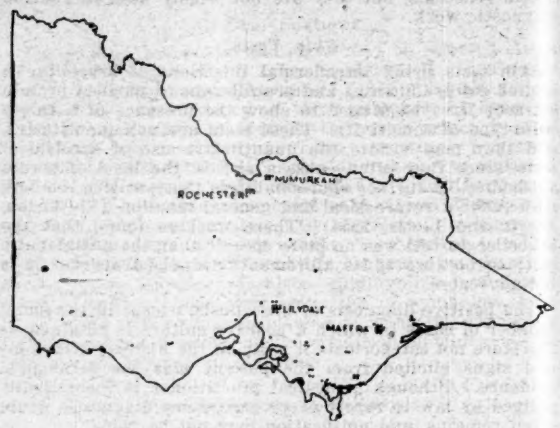

FIGURE III.

Distribution of extra-metropolitan cases of brucellosis, 1954-1956.

It is evident from the foregoing that, although brucellosis in man is a notifiable disease in Victoria, only a proportion of diagnosed cases are notified, and hence the official figures are not a reliable index of the incidence of the disease.

Then again, there is almost certainly a considerable collection of cases which escape diagnosis simply because the possibility of brucellosis is not considered. In any case of vague ill-health, with or without evident pyrexia, the patient should be examined serologically for brucellosis, both the direct and the antiglobulin test being used. Because of the possibility of a fluctuating titre, the tests should be repeated if the findings are in any way suspicious.

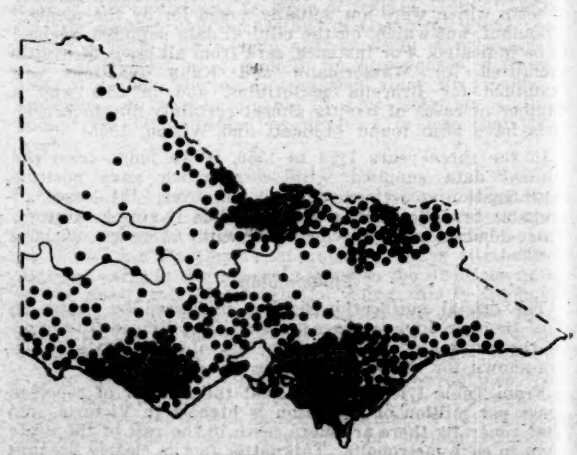

FIGURE IV.

Distribution of dairy cattle, 1955. (One dot represents 2000 head.)

In the present series of 121 cases, seven patients presented with inflammation of the uveal tract of the eye, so

that a routine Brucella agglutination test on such patients is indicated just as strongly as a routine Wassermann test.

There is no doubt that this infection is frequently an occupational hazard to which those who handle cattle are exposed, and that the eradication of brucellosis in man would follow if all infected cattle could be destroyed. At present vaccination of heifers with live strain 19 is being relied on to combat contagious abortion, regardless of the fact that, though this organism may be relatively innocuous in cattle, it is by no means non-pathogenic to man.

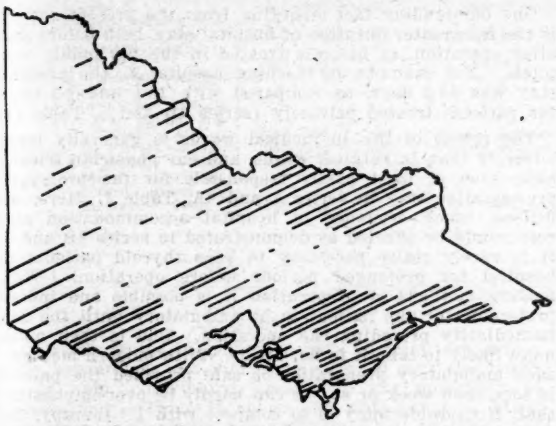

FIGURE V.
Shading represents dairying districts in which brucellosis has not been found.

In computing the economic cost of brucellosis to the community, the analogy of the iceberg should be remembered, and it may well be that more than seven-eighths of the problem still lies hidden beneath the surface. Radical measures of test and slaughter of infected cattle are being tried in Tasmania and on a herd scale in certain areas on the mainland of Australia. To make such measures universal, with government compensation, would be expensive and politically difficult; at present the cost is thought to outweigh the losses due to contagious abortion with its sequelæ of lowered milk production and unthriftiness in our dairy herds. However, those who have to decide whether we can afford to let the fires of brucellosis smoulder on indefinitely should also cast into this balance the enormous loss of man-hours and human efficiency resulting from human brucellosis.

Summary.

1. Human brucellosis has been a notifiable disease since 1937.

2. In 20 years the number of cases notified has risen from one to over 20 per year.

3. The official figures are not a reliable index of the incidence of brucellosis.

4. Diagnosis usually depends on a diverse and often vague clinical picture supported by the direct and indirect (antiglobulin) agglutination test. Skin testing is not advocated.

5. One hundred and twenty-one probable cases diagnosed in the years 1954 to 1956 in the Public Health Laboratory, University of Melbourne, are reviewed.

6. The epidemiology suggests that infection is most often acquired directly by those who handle infected cows, though milk-borne infection may also occur.

7. Cases are brought to light only if the medical attendant is alive to the possibility of brucellosis — *i.e.*, is brucellosis-minded.

8. The suggestion is made that the practicability of eradicating the disease from dairy cattle by a test and slaughter policy be considered, and that the cost be weighed against the economic loss to the community resulting from human disease *plus* the reduction in agricultural returns.

Acknowledgements.

My thanks are due to members of the staff of the Public Health Laboratory who have taken part in this work, to the many Victorian practitioners who have furnished the sera and clinical data, and to those who have provided information, including the Directors of the State Health Departments, the Chief of the Animal Health Division of the Commonwealth Scientific and Industrial Research Organization, and the Superintendent of the Dairying Division of the Victorian Department of Agriculture.

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THYROIDECTOMY: A SURVEY OF CURRENT HOSPITAL MORTALITY AND MORBIDITY.

By F. F. RUNDLE, M.D., F.A.C.S.,[1] AND J. S. INDYK, F.R.A.C.S., F.R.C.S.,
Sydney.

Now that radio-iodine therapy is freely available for the patient with thyrotoxicosis, it is timely to examine the mortality and morbidity rates of surgical thyroidectomy. This is so because radio-iodine and surgery are competing methods of treatment, and the physician's choice must be influenced by the standard of the radio-iodine and surgical services available for his use. In this paper we present data from five series of thyroidectomies, four carried out in New South Wales under different circumstances, and, for comparison, a fifth from a thyroid clinic in New York State, United States of America.

[1] Work aided by a grant to the Unit of Clinical Investigation, Royal North Shore Hospital, from Sir Edward Hallstrom.

Methods.

Data were collected from two Sydney teaching hospitals (series 1 and 2), from a large provincial hospital providing post-graduate training facilities (series 3), and from two practices, the first (series 4) a general surgical practice in which thyroid operations, though the subject of special study, comprised only about 20% of operations performed during the period under review, and the second (series 5) a practice confined solely to thyroid surgery. The records of all patients were examined, and note was taken of the name, age, diagnosis, duration of pre-operative and post-operative stay, and complications noted in hospital for each. The information so obtained is summarized in Tables I and II.

All thyroidectomies performed during the years stated in Table I have been included, with the sole exception of intrathoracic thyroidectomies requiring sternal splitting or thoracotomy procedures. It may be accepted that such operations in elderly people (in whom intrathoracic goitre characteristically occurs) carry an altogether different order of risk from standard cervical thyroidectomy.[1] Moreover, I^{131} therapy is usually ineffective in such goitres, the symptoms of which are mechanical in character.

No attempt has been made to distinguish between the mortality and morbidity of thyroidectomy for toxic goitre on the one hand and for non-toxic goitre on the other. Since the hazard and morbidity of operation for toxic goitre (to which alone I^{131} therapy is applicable) must clearly exceed those for non-toxic goitre, the results, in so far as the comparison between I^{131} therapy and surgery is concerned, must be biased in favour of surgery.

It should be emphasized that only complications noted in hospital have been included. Inevitably many recurrent nerve palsies and possibly even a few instances of parathyroid tetany may have been overlooked. The frequency of recurrent thyrotoxicosis and post-operative hypothyroidism has not been determined in these series. Such complications become evident only some months afterwards.

Results.

Mortality Rate of Thyroidectomy.

In teaching hospital X, two deaths occurred in quick succession from post-operative hæmorrhage midway through 1956, and inclusion of the 1956 data would undoubtedly have raised the death rate slightly. But in hospital Y there was no death after thyroidectomy in 1956. The current mortality rate in these two metropolitan teaching hospitals is therefore of the order of 2%. In the provincial hospital it was 5·5%, though the number of operations performed was too small to establish an exact figure firmly. But, again because of the few operations carried out, this death rate is unlikely to fall unless thyroidectomies are concentrated in the hands of one surgical team.

Conversely, in very practised hands the mortality rate of thyroidectomy falls to vanishing point (cf. series 4 and 5, Table I). Similarly, Thorén and Wijnbladh (1956), collecting information concerning the mortality of thyroidectomy in leading clinics of various countries, found that it ranged from nil to 0·47% in nine series numbering from 180 to 3660 cases. But this low rate would not be a gain if efficiency were attained only at the cost of doing a lot of unnecessary operations; it is clearly less risky to resect minimal thyroid enlargements than to operate on grossly pathological goitres. Our colleague, Dr. John McClintock, has not informed us of the operation rate in his clinic, but in our own practice for the years 1955 and 1956 the percentages of all "thyroid" patients operated on were 27 and 23 respectively. This probably indicates the general level for previous years, the data from which, however, are not readily available.

Careful preparation, a slow, painstaking technique, teamwork at operation, expert anæsthesia and observant nursing are the chief ingredients of a nil mortality rate. Deaths from operative hæmorrhage are clearly due to inadequate surgery and blood replacement. Less generally recognized is the vital importance of early tracheotomy when severe post-operative wound swelling is associated with stridor, as emphasized by Lahey and Hoover (1951). All our own patients have been seen beforehand by a physician. We believe that a physician's help is invaluable in the selection of patients and in the management of "bad risk" cases.

Duration of Hospital Stay.

One outstanding fact emerging from the present survey is the far greater duration of hospital stay, both before and after operation, of patients treated in the big public hospitals. For example, in teaching hospital X, the average stay was 23·6 days, as compared with 10·1 and 6·2 days for patients treated privately (series 4B and 5, Table I).

The *tempo* of life in medical wards is generally more leisurely than in surgical wards, and our physician friends have been at least partly responsible for the prolonged pre-operative stay in series 1 and 4A, Table I. Here, we believe, much economy in hospital accommodation and costs could be effected as demonstrated in series 4B and 5. It is rarely really necessary to keep thyroid patients in hospital for prolonged periods before operation. With modern methods of preparation it is possible and indeed preferable for the patient to be ambulatory until the day immediately preceding the operation. She is then much more likely to take it in her stride. With modern methods, such ambulatory preparation is safe provided the patient is seen each week or so. It can hardly be over-emphasized that, if thyroidectomy is to compete with I^{131} therapy, the duration of hospital stay must be reduced to the point where it is no longer a major economic and social factor.

The duration of the hospital stay after operation is, of course, a rough yardstick of the morbidity rate. Thus where patients have been discharged after six or seven days we may presume that they have escaped major complications. One of the chief bugbears prolonging the hospital stay is post-operative hæmatoma. It is certain that we should give more time to hæmostasis. If the surgeon gives ten more minutes to the operation, he may well save the patient an additional week in hospital. Minor wound hæmatomas and infections have been all too numerous in these series, but have not been specially noted in Table II.

Significance of Hospital Stay in Management.

The average duration of hospital stay for thyroidectomy in our large public hospitals is more than twice that for patients in series 4B and 5. Thus the cost to the community of thyroidectomy in general hands is more than twice as great as it should be; or in other words, the same number of patients could, if the necessary arrangements were made, be treated in one-half the number of beds. The chief changes necessary would be (*a*) more careful scrutiny of admission (in relation to scheduled date of operation) and discharge of patients, and (*b*) concentration of the operations in fewer hands. In this connexion, the operations in series 1, 2 and 3 were performed by no fewer than 13, 8 and 5 different surgeons respectively. Finally, the surgical team responsible for the thyroidectomy should supervise the patient's preparation before her admission to hospital. As with most standard surgical procedures, elaborate physical facilities are not necessary for thyroidectomy. Thus the operations included in series 4B were carried out in 16 different hospitals; over 60% were performed in 15 small private hospitals where the theatre and ward accommodation is less elaborate and certainly a great deal less costly than that in the great public hospitals.

We do not know how the results of fact-finding surveys of other standard surgical procedures would compare with those here stated for thyroidectomy; but the matter should be one of interest for hospital administrators and politicians to pursue in this State, where the constant and almost universal call is for bigger and more elaborate hospitals.

[1] During the periods under review, deaths occurred from intrathoracic thyroidectomy with sternal splitting in both McClintock's (one case) and Rundle and Indyk's series (one case).

TABLE I.

Mortality and Morbidity of Thyroidectomy.

Series Number.	Hospital or Surgical Practice.	Years Operations Performed (Inclusive).	Number of Operations.	Surgeon.	Number of Deaths.	Duration of Hospitalization (Days).					Complications Noted in Hospital (Number %).
						Pre-operative. Average.	Pre-operative. Range.	Post-operative. Average.	Post-operative. Range.	Total: Average.	
1	Sydney teaching hospital X	1953–1955	232	13 different surgeons.	3 (1·3%)	10·4	1–92	13·2	0–55	23·6	25 (10·8%)
2	Sydney teaching hospital Y	1953–1955	83	8 surgeons.	2 (2·4%)	4·6	1–27	9·0	0–26	13·6	10 (12·0%)
3	Provincial hospital in N.S.W.	1953–1955	36	5 surgeons.	2 (5·5%)	4·6	1–48	10·5	2–30	15·1	5 (13·8%)
4	A general surgical practice:										
	(*a*) Clinic patients in public hospital	1951–1956	74	Present authors.	0	8·3	1–101	9·3	4–29	17·6	17 (4·5%)
	(*b*) Private patients	1951–1956	305	Present authors.	0	1·8	1–21	8·3	3–49	10·1	
5	A thyroid clinic (Albany, New York, United States of America), "private"	1953–1955	747	J. C. McClintock.	0	1·5	1–20	4·7	3–20	6·2	45 (5·8%)
Total	.. ..	—	1477	—	7	—	—	—	—	—	85

Complications.

As already stated in connexion with hospital stay, minor wound hæmatomas and infections occurred very frequently and, in sum, contributed greatly to the morbidity of thyroidectomy. Table II shows the wide range of other important complications following the total of over 1500 thyroidectomies. Most of these complications are remediable if recognized and correctly treated.

Of special interest are parathyroid tetany and recurrent nerve damage. They are direct local consequences of the operation. It is certain that their frequency can be reduced to vanishing point by meticulous surgery.

Permanent parathyroid tetany is the most serious long-term complication of the local surgery. The relatively high frequency of tetany in McClintock's series is out of step with the excellence of his results otherwise. He states: "One thing that impressed me during this survey, was the frequency with which parathyroid tetany was encountered. . . . As a result of this analysis I am now leaving a margin of capsule and gland posteriorly on one side at the least. . . . I see no reason why the frequency cannot thus be reduced."

Summary and Conclusions.

1. The mortality of thyroidectomy in the two Sydney teaching hospitals surveyed is of the order of 2%. In a large country hospital in New South Wales it is approximately 5%. In the teaching hospitals the complications rate (minor wound hæmatomas and infections excluded) is about 11%, and in the country hospital 14%. As thyroidectomies for simple goitre were included, these figures probably understate the mortality and morbidity rates of thyroidectomy for thyrotoxicosis. The average

TABLE II.

Thyroidectomy: Post-Operative Complications.

Post-Operative Complications.	Teaching Hospitals.		Provincial Hospital.	Rundle and Indyk.	McClintock.
	X.	Y.			
Recurrent nerve paralysis	10 (including 4 bilateral)	3 (2 bilateral)	—	2	7
Tetany:					
Transient	—	—	—	2	15
Permanent	3	2	—	—	12
Asphyxia	4 (3 fatal, 1 relieved by tracheotomy)	—	—	—	—
Post-operative hæmorrhage; reoperation for hæmorrhage or wound sepsis.	3	2 (1 fatal)	2	9	6
Respiratory, including pneumonia	4	2	2 (1 fatal)	1	4
Permanent visual disturbance due to blood loss ..	1	—	—	—	—
Fatal thyroid crisis	—	1	—	—	—
Wound sepsis, fibrinous pericarditis, pleural effusion	—	—	1 fatal	—	—
Acute dilatation of stomach	—	—	—	—	1
Coronary occlusion	—	—	—	1	—
Confusional state	—	—	—	2	—
Total	25 (10·8%)	10 (12·0%)	5 (13·8%)	17 (4·5%)	45 (5·8%)

duration of hospital stay for thyroidectomy varied from 15 to 24 days.

2. In the hands of specially trained teams, the mortality rate of thyroidectomy approaches nil, and the frequency of important complications is of the order of 5%. The total duration of hospital stay is six to ten days.

3. An incidental finding of this survey was that the management of patients undergoing this standard surgical procedure in the large public hospitals was uneconomical.

4. Provided a good radio-iodine service is available, I^{131} therapy of thyrotoxicosis is virtually free of risk and morbidity. The present survey thus greatly favours a rapid increase in its use in preference to thyroidectomy in general hands. On the other hand, where special surgical facilities are available, operation is still a reasonable alternative therapeutic tool.

Acknowledgements.

For their generous help with the survey we are greatly indebted to Dr. John McClintock, Dr. Norman Newman, Dr. Peter Harvey and Dr. Peter Blaxland, and to Mrs. W. Ireland.

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EPILEPSY IN CHILDHOOD.

By ERIC DAVIS,
Sydney.

EPILEPSY has been described as a paroxysmal and transitory disturbance of the function of the brain, which develops suddenly, ceases spontaneously and exhibits a conspicuous tendency to recurrence (Russell Brain, 1955). It is a symptom resulting from abnormal neuronal discharge.

Epilepsy, be it either motor or sensory, focal or generalized, with or without loss of consciousness, or be it described as psychic seizures of temporal lobe origin, may occur in childhood under the following sets of circumstances: (*a*) as the centrencephalic or so-called idiopathic epilepsies—*viz.*, *grand mal* and *petit mal*; (*b*) associated with infantile cerebral palsy; (*c*) in the child who has suffered post-natal brain damage or injury; (*d*) associated with fever, acute infections and possibly dentition—the febrile convulsive group.

The evaluation of the infant or child who presents with a history of epileptiform seizures is a problem of considerable interest and some complexity. It is a problem that is commonly faced by the general practitioner in the home, and by the physician in out-patient departments or in the consulting room. Whenever a seizure occurs, it does so as a distressing and frightening episode to the parents; there are few other emergencies in childhood which will bring the young patient faster to the doctor or the doctor faster to the patient.

The Centrencephalic Epilepsies.

With the advances of electroencephalography and the intense research by such leaders in the field as Penfield and Jasper, Drooglever-Fortuyn *et alii*, one accepts the proposal that such cerebral dysrhythmias are the result of a discharge of neurons in the central grey matter of the brain—the higher part of the brain stem, the reticular nuclei, the *massa intermedia* and the nuclei of the thalamus.

What motivates the electrical discharge is not known; when it is known, then the term "idiopathic" will disappear, and this type, as the others, will be placed in the category of symptomatic epilepsy.

It is my opinion that epilepsy in childhood (with the exception of *petit mal*—and even this, too, may one day be included) is synonymous with the term "epilepsy in the brain-damaged child". It is further my opinion that epilepsy which manifests itself before puberty is rarely, if ever, idiopathic. If one searches hard enough, some reason or explanation can be found.

Centrencephalic epilepsy (excluding pure *petit mal* with its three cycles per second spike-and-wave discharge on a normal electroencephalographic background) finds its peak of onset in the immediate post-pubertal years—namely, fourteen to sixteen. As it is my intention to discuss epilepsy in childhood, with particular reference to brain damage, I propose to say no more about the centrencephalic group, but to pass to a consideration of the second group in my classification.

TABLE I.

Ætiology of Brain Damage.	Number with Epilepsy.	Spastics.	Athetoids.	Ataxics.	Abnormal Electro-encephalo-grams.
Dystocia ..	43	34	6	3	42
Cerebral anoxia	20	9	11	—	18
Prematurity ..	13	12	1	—	11
Pre-eclamptic toxæmia and hypertension	11	9	1	1	11
Rh incompatibility ..	6	—	6	—	6

Epilepsy in Infantile Cerebral Palsy.

The clinical material for this particular presentation has been obtained during the years 1944 to 1956, during which period I was (and I still am) engaged in the investigation of this problem at The Spastic Centre, Sydney.

Infantile cerebral palsy may be defined as a condition characterized by a motor deficit or defect—paralyses, weakness, incoordination, hyperkinesia or any other type of motor aberration—due to involvement of the motor centres of the brain (Perlstein, Gibbs and Gibbs, 1955).

The patient with infantile cerebral palsy needs no lengthy description. The deficit or defect may be so mild as to be scarcely noticeable, or so severe as to produce the familiar picture of the quadriplegic or hemiplegic child or the child with the endless grimacing and writhing of athetosis. To describe in detail the varieties of cerebral palsy is beyond the scope of this paper.

Children with cerebral palsy may be divided into the following three general categories (again to quote Perlstein, Gibbs and Gibbs and to use the classification in vogue at The Spastic Centre): (i) those with spasticity—the spastic hemiplegics, the quadriplegics, the triplegics and the paraplegics; (ii) the dyskinetics—the athetoids, children with athetosis, rigidity and/or tremors—presumably owing to extrapyramidal involvement; (iii) the ataxics—the third general group, often with hypotonia, and by far the smallest group; this comprises those children in whom dyssynergias and balance difficulties are predominant.

In the cerebral palsied population as a whole, the percentage distribution in the above classification has been variously quoted. Perlstein, Gibbs and Gibbs give the following figures: spastics 68%, athetoids 22%, other dyskinetics 6%, ataxics 4%. Our figures at The Spastic Centre in Sydney correspond closely to these.

During the period mentioned earlier, a survey of 700 infantile cerebral palsied subjects was carried out. From this number 93 children with cerebral palsy and epilepsy have been carefully studied. This group selected for study had moderate, good or normal intelligence. They attended either normal school or school at The Spastic Centre. Every child from this group has been clinically evaluated

and subjected to psychometric testing, and has been subjected to one or more electroencephalographic examinations. From this particular group I have excluded cerebral palsied epileptic children with mental retardation or with such cerebral defect as to prevent their being a clinical problem. In this category, therefore, I have excluded such conditions as microcephaly, craniostenosis, hydrocephaly, the agenesias and rigidities, and mental defect.

The epileptic manifestations of the cerebral palsied child have some rather special characteristics, and I should like to spend a little time talking about them. One of the earliest epileptic manifestations is the infantile spasm, in which the young baby suddenly twitches all

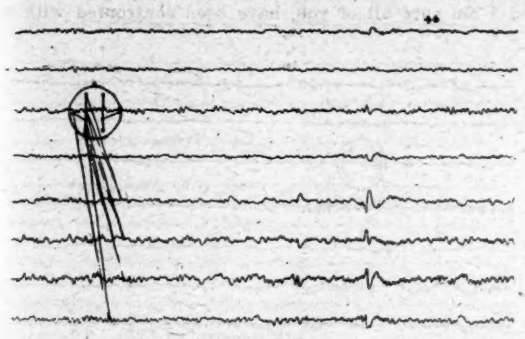

FIGURE I.

Female patient, aged eight years. Right spastic hemiplegia. Maternal dystocia. Jacksonian attacks; left-sided focal spikes.

over, changes colour, rotates his eyes upwards and then relaxes, or develops a tonic muscular spasm, arches his back and then relaxes when this minor convulsive episode is over. Such infantile spasms are a common clinical precursor or a warning sign of brain damage, and the full picture of cerebral palsy may later develop. Infants with such spasms have a classical electroencephalogram—the hypsarrhythmia of Gibbs and Gibbs.

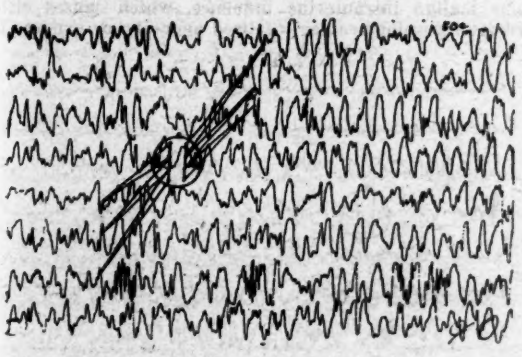

FIGURE IIA.

Female patient, aged eleven years. Right spastic hemiplegia. Mother suffered from pre-eclamptic toxæmia. *Grand mal* and *petit mal*. Left-sided focal spikes. Seizure activity before treatment.

A little later in the picture, another type of seizure activity manifests itself. This is the so-called *petit mal* quartette, so named by Lennox and Jean Davis. The various components of this quartette are as follows: (i) the classical *petit mal* or absence, five to thirty seconds in duration, in which the only motor concomitant may be a rhythmic minor twitching or head movement; (ii) the astatic or "drop" or "salaam" or inhibition epilepsy, in which head nodding, falling and limp collapse are typical features; (iii) the lightning-like myoclonic jerk with flexion of the arms; (iv) the massive myoclonic jerk with jack-knifing of the body. Components (ii), (iii) and (iv) are usually associated with the "slow" two cycles per second blunt spike and slow recovery wave complex discharge. This was originally called *petit mal* variant epilepsy by Gibbs, H. Davis and Lennox. Periods of sudden stillness, staring, sagging, small jerkings or mild tonicity, often without full loss of consciousness, are commonly the clinical correlates of a serial discharge which is recorded in the electroencephalogram. This two cycles per second spike-and-wave discharge suggests neuropathological damage.

In common with other workers in the field, I have found that the broad spike and slow wave, occurring either

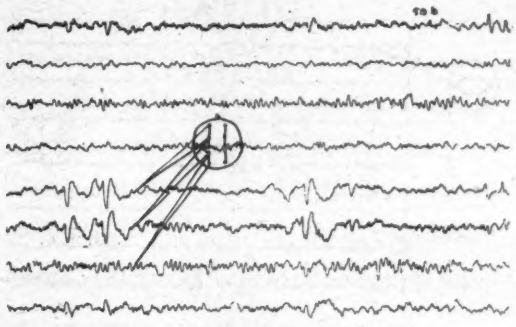

FIGURE IIB.

Same patient as in Figure IIA, after treatment.

singly or as a serial two to four cycles per second seizure discharge, is the outstanding, the most distinctive and prognostically the most informative electroencephalographic abnormality. A single spike discharge with its hump may or may not be accompanied by a contraction of the muscles (myoclonic jerk). A brief discharge of five to ten seconds may be associated with a fall or head nodding.

The child with cerebral palsy and epilepsy is a brain-damaged child. Throughout this presentation, I have used

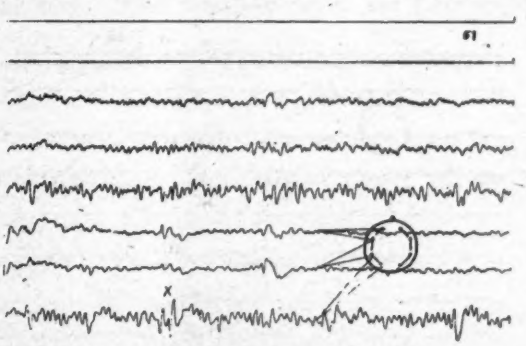

FIGURE III.

Female patient, aged eight years. Right spastic hemiplegia, anoxia, focal fits, left focal spikes.

the term "damaged" (or as some call it "brain injured") somewhat loosely, and in a wide sense, to embrace the pathological changes that result from many known and unknown influences which damage or inhibit the development of the brain of the unborn child or injure the brain of the child during the natal process. Whatever noxious influences are at work, the result is cerebral defect. This may be massive in agenesis and microcephaly, lobar in atrophic lobar sclerosis or confined to smaller areas of cortical damage as in tentorial indenting of the temporal lobes. Direct natal trauma may cause cortical damage, gliosis and atrophy. Anoxia of ante-partum hæmorrhage

or of prolonged labours may likewise result in neuronal death with scattered areas of gliosis and atrophy. The resultant area of damage to the cortical mantle is revealed in the electroencephalogram, and such areas are commonly epileptogenic.

Five major noxious influences have clearly emerged from this survey as a cause of cerebral palsy and epilepsy. These are: (i) dystocia; this includes instrumental deliveries, prolonged labours and post-maturity; (ii) cerebral anoxia; (iii) prematurity; (iv) pre-eclamptic toxæmia and maternal hypertension; (v) Rh incompatibility. Of the 700 children surveyed, with all forms of cerebral palsy, the selected group of 93 had epilepsy

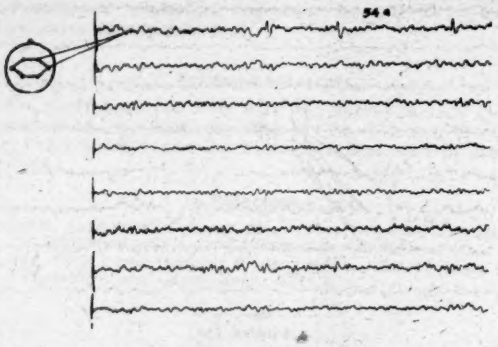

FIGURE IV.

Male patient, aged eight years. Left spastic hemiplegia, prematurity, left Jacksonian fits, right-sided spikes.

as a direct result of brain damage—a proportion of 13%. Many more were epileptics; but as I stated before, they did not present a clinical problem. Actually, 40% of our cerebral palsied population had had one or more seizures (Perlstein, Gibbs and Gibbs, 47%). From this it will be seen that brain damage not only produces motor defect, but also produces epilepsy.

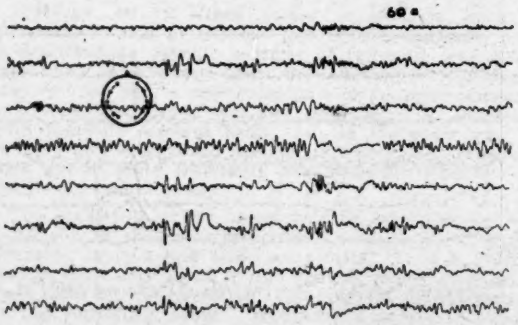

FIGURE VA.

Male patient, aged ten years. Right-spastic hemiplegia. Maternal dystocia. *Grand mal*. Before treatment.

An analysis of this group of 93 is interesting. It will be seen that epilepsy is more common in spasticity than in other forms of cerebral palsy. The actual dissection is shown in Table I.

An analysis of the type of clinical seizures in this group of 93 is also not without interest. They may be set out as follows, with the figures of Perlstein, Gibbs and Gibbs in parentheses:

Grand mal, 40—43% (53%).
Focal and Jacksonian seizures, 23—24% (24%).
Petit mal quartette, 13—14% (8·6%).
Grand mal and others, 15—16% (14%).
Psychomotor, 2—2% (0·4%).

The figures of Perlstein, Gibbs and Gibbs correspond closely with the results at The Spastic Centre. In the foregoing analysis you will note several interesting facts. First, the incidence of *petit mal* quartette epilepsy, which, as I said before, is a feature of the epileptic cerebral palsied child, is 14%. Secondly, it is also interesting to note that *grand mal* and *grand mal* mixed reach a total of 59%. In an unselected epileptic population in childhood, simple *petit mal* is by far the commonest form of epilepsy, with a total of 60% and over (Gibbs and Gibbs).

In addition to the obviously cerebral palsied child, I, and I am sure all of you, have been confronted with the

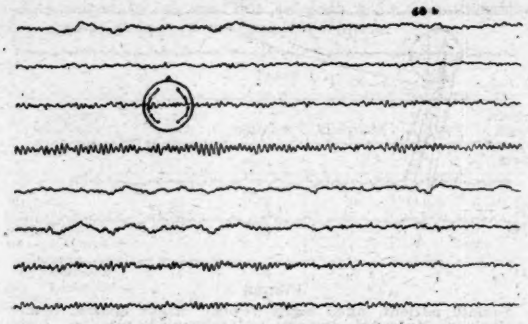

FIGURE VB.

Same patient as in Figure VA, after treatment.

problem of the child who has convulsive seizures, and yet has no obvious motor defect, but whose history would lead to the suspicion that some malign influence has been at work. In a small series of my own of children with epilepsy without motor defect, I have found the common denominator of prematurity. I am more and more convinced that prematurity exposes the brain of the baby to some malign intrauterine influence, which causes either arrest of development or localized agenesis, or exposes the

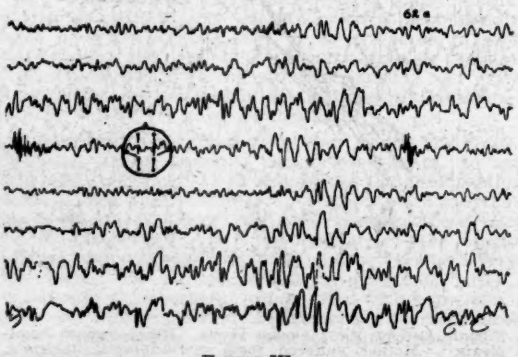

FIGURE VIA.

Female patient, aged nine years. Right spastic hemiplegia. Maternal dystocia. *Petit mal* quartette epilepsy, spikes and spike and slow waves, *petit mal* variant. Before treatment.

delicate brain to ready damage during the birth process. In either case epileptic zones are created, and these are readily recorded in the electroencephalogram of the baby or child who has seizures.

The photostat reproductions (Figures I to IX) are added to illustrate the electroencephalographic findings. The incidence of abnormal electroencephalograms is almost 100%. In these brain-damaged children with epilepsy, the

following are the common electroencephalographic abnormalities found in the interseizure records: (i) focal spikes, (ii) focal spikes with a spike and slow wave focus, (iii) diffuse spikes, (iv) multifocal spikes, (v) the *petit mal* variant seizure discharge of Gibbs and Gibbs. This is the slow two to four cycles per second spike and slow wave discharge described by numerous writers as the correlate of brain damage. The spike and slow wave complex appears to be the *sine qua non* of cortical or subcortical atrophy; the focal spikes indicate more superficial damage. Seizure activity of the *petit mal* variant type is a correlate of extensive neuropathology.

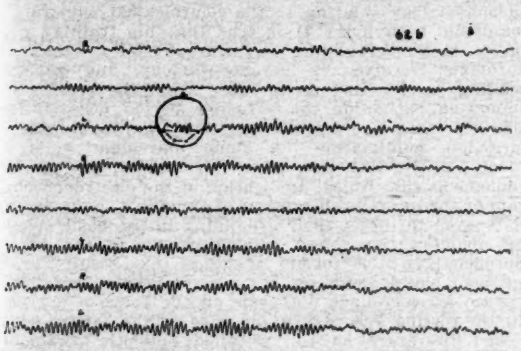

FIGURE VIB.
Same patient as in Figure VIA, after treatment.

Epilepsy in the Child with Acquired Post-Natal Damage.

This presentation will deal briefly with epilepsy that presents as a problem in the child who, normal at birth, has been subjected to some later noxious influence that has resulted in brain damage and subsequent epilepsy. The material for this has again been culled from the Royal North Shore Hospital of Sydney, The Spastic Centre and my own private practice. In this group I include the following ætiological subgroups.

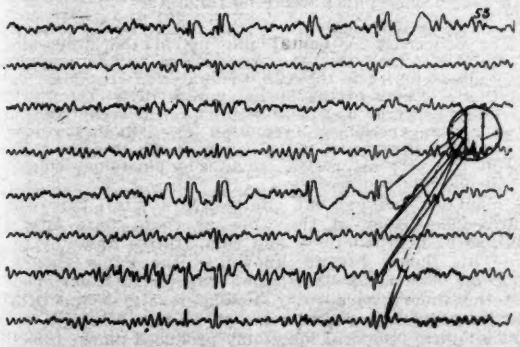

FIGURE VII.
Male patient, aged five and a half years. No motor defect. Prematurity. Neonatal and right Jacksonian attacks. Note focal spikes and spike and slow waves.

Post-Natal Trauma.

There were nine cases due to post-natal trauma—a very small personal series, admittedly—during 1955 and 1956. A few comments are pertinent. The first relates to the important fact of time relationship. I have noted—and, of course, in this I am not alone—that the period between the injury and the actual onset of seizures is extremely variable. Periods of seven years or more are not uncommon between the time of accident and the first seizure. Secondly, epileptogenic zones in the brain mantle may be created after both open and closed head injuries. Thirdly, and commonly, the first seizure is a nocturnal one. The variety of seizure varies with the site of maximal damage. The tell-tale broad spike or spike and slow wave complex is almost invariably to be found in these young children with post-traumatic epilepsy.

Infection.

Encephalitis, polioencephalitis and meningitis are the commonest ætiological factors in the infection group. Rarely osteomyelitis of the skull may result in cortical

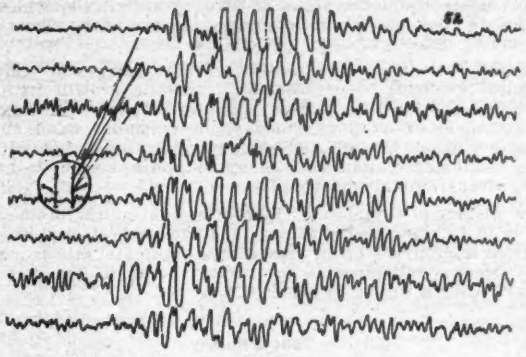

FIGURE VIII.
Male patient, aged seven years. No motor defect. *Petit mal* variant discharges (arising left side). Adversive seizures to right.

suppuration and scarring—I have one such case. This group included 18 children; the commonest ætiological factor was encephalitis. Some of these had no motor defect. The second commonest factor in the ætiology of post-infective epilepsy is meningitis.

Lead Encephalopathy.

A very small personal series of three patients of my own examined in 1956 are included in the lead encephalopathy group. These three children all had a history of

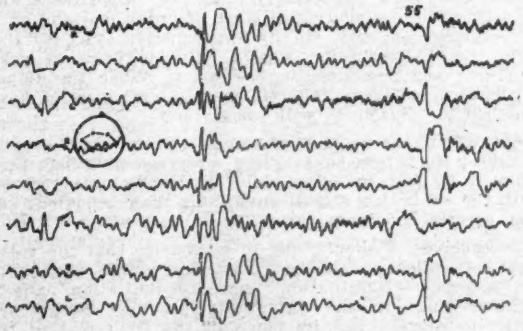

FIGURE IX.
Male patient, aged six years. Right spastic hemiplegia, anoxia, *petit mal* quartette epilepsy—drop attacks and myoclonic jerks. Short serial discharge.

exposure to lead; all had epilepsy and, indeed, presented as epileptics for investigation. Urinary lead studies, X-ray examinations of bones *etc.* all gave positive results, and diagnostic titres of lead excretion were confirmed by the Government laboratories. "Versene" and anticonvulsant therapy proved to be efficient medication.

Comment.

It is not my intention to deal with the question of febrile convulsions in infancy and the pre-school child.

Wilfred Cary has discussed this very satisfactorily (Cary, 1956).

Thus it may be seen that the clinician may be confronted with four diagnostic problems when he sees the child for the first time during or after a convulsion. Adequate evaluation of the pre-natal history and of the events of the confinement and a post-natal history will help determine the ætiology.

Brain damage to the child *in utero* or during the birth process may cause cerebral palsy. The cerebral defect may become epileptogenic. Brain injury may result in very small and focal areas of atrophy or gliosis, which, although they become epileptogenic, do not cause somatic or motor defect.

Some patients with infantile cerebral palsy will show clinical evidence of depression of somatic growth in an affected limb or limbs. For example, a young child may show facial or skull asymmetry, or a smaller hand and arm or leg on the affected side, together, of course, with the usual concomitants of an upper motor neuron lesion or extrapyramidal abnormality.

A history of trauma may help in evaluating the problem. It is to be remembered that a meningo-cerebral cicatrix, a buried microgyrus or an area of post-traumatic gliosis may not become epileptogenic for periods of up to five or ten years after a forgotten accident.

Conclusion.

It may seem pointless to make electroencephalographic examinations of the brain-damaged cerebral palsied child; but there are many problems that confront the clinician or staff of such a centre as The Spastic Centre. Overt seizures add to the problems of management, and a recognition of the electroencephalographic pattern has enabled some guidance to be given in therapy. It is a well-known fact that *grand mal* and *petit mal* in the cerebral palsied child respond poorly to medication; but one thing did emerge from this study—namely, the value of the diones in the treatment of the two cycles per second dysrhythmias. Whilst by no means comparable with their effect on the three cycles per second dysrhythmias, they were responsible for the reduction of many of the seizures associated with this two cycles per second or *petit mal* variant seizure activity. Other anticonvulsants have, of course, been used, particularly "Dilantin" when there was (and this was common) a mixture of *grand mal* and *petit mal* quartette epilepsy. In my own experience, I have also found that "Mesontoin" was a valuable drug in post-traumatic and post-infective epilepsies. When the diones have failed or have produced blood disturbances, I have switched to "Mysoline" with good results.

Apart from the overt seizures, the cerebral palsied child is subject to severe behaviour disorders, and it has been common to find in these children dysrhythmic records. With the exhibition of anticonvulsants their behaviour has been greatly improved.

To conclude, I should like to emphasize that the treatment of epilepsy does not start and finish with anticonvulsants. "Habilitation" and "rehabilitation" and a rightful place in the community all play their part. Epileptic surgery has its place in the treatment of the uncontrolled epileptic.

Acknowledgement.

Due acknowledgement must be made to Dr. Claudia Burton-Bradley, Medical Director of The Spastic Centre, without whose drive and cooperation this study could not have been carried out.

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INTERICTAL EVENTS IN THE CHILDHOOD EPILEPSIES: THEIR PSYCHIATRIC SIGNIFICANCE.[1]

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TONIGHT I want to consider what contributions, if any, the psychiatrist can make to the problem of the childhood epilepsies. This question immediately raises another: what has the psychiatrist learned from the recent advances in neurophysiology relating to the neurological substrate of organismic behaviour? It is true that his training gives him a better grounding in neurophysiology than the neurologist receives in psychopathology, and generally speaking psychiatrists know more about the processes of summation, extinction, the refractory period, negative feedback, *etc.*, than neurologists appreciate the significance of repression, sublimation, let alone individuation of the archetypes. Nevertheless, when it comes to such practical problems as the clinical application of the electroencephalogram or the interictal behaviour of epileptics, many psychiatrists seem to forget their grounding in the basic sciences and abandon themselves wholeheartedly to the empiric approach. In the former instance this results in the unreasonable demand on the electroencephalographer to produce a ready-made diagnosis on the basis of a twenty-minute resting record. In the case of the latter, we get a vast literature on the so-called epileptic personality, ignoring the fact long known to neurologists and neurophysiologists that epilepsy is no unitary condition but a variety of states, each characterized by "spontaneous, self-sustained hypersynchronous discharges of nerve impulses of high frequency spreading synaptically and ephaptically" (to use Gastaut's definition), but affecting different brain areas and different brain systems. It is precisely the localization of these abnormal discharges that is of interest, not only to the surgeon who seeks to extirpate lesions and thereby suppress foci, but also to the psychiatrist who hopes to understand some of the interictal behaviour abnormalities in the light of the particular brain system or systems involved. In order to know what behaviour effects we have to look for, it will be necessary for me to summarize the experimental evidence in this field.

In 1937 James Papez wrote as follows:

> The central emotive process of cortical origin may be conceived as being built up in the hippocampal formation and as being transferred to the mamillary bodies and then through the anterior thalamic nuclei to the cortex of the *gyrus cinguli*. The cortex of the cingular gyrus may be looked on as the receptive centre for the experience of emotion. . . . Radiation of the emotive process from the *gyrus cinguli* to other regions in the cerebral cortex would add emotional colouring to psychic processes.

As MacLean pointed out twelve years later, this was a courageous theory at the time, as there were only the findings of neuroanatomy and comparative anatomy to go on. This theory became known as the Papez theory of emotion. The early extirpation experiments designed to test the theory gave contradictory results. Thus Klüver and Bucy, in their experiments on macaca monkeys, found that bilateral temporal lobectomy produced marked docility and hypersexuality in a particularly aggressive group of these animals. They thought that the results were due to interruption of Papez's circuit at the hippocampal level. Next year, however, Spiegel, Miller and Oppenheimer, working with dogs and cats, produced the opposite result on extirpating various parts of the rhinencephalon, such as the olfactory tubercle, the hippocampal formation and especially the amygdala. Bard and Mountcastle, in a series of carefully planned experiments on cats, got an enhanced rage reaction on removing or damaging the hippocampal-fornix formation and especially the amygdala, thus confirming the findings of Spiegel, Miller and Oppenheimer. This rage reaction differs from the sham rage of the hypothalamic animal, in that the aggression is well directed

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on April 24, 1957.

and coordinated owing to the intactness of the neo-cortex. However, a similar result can be obtained by a bilateral lesion of the ventro-medial nucleus of the hypothalamus —the so-called Wheatley cat.

Apart from the possibility of species differences, which is supported by the experiments of Margaret Kennard on the cingulate area, there is the alternative that more than one system of functionally related brain structures is contained in the non-olfactory portion of the rhinencephalon or "visceral brain" or limbic lobe. The connexions are exceedingly complex, and apart from the cingulate gyrus, the medial and posterior orbital cortex, the anterior insula and the temporal pole are cortical areas that are involved. These areas are described as the mesopallium by MacLean and his co-workers, who contrast them with the archipallium, the hippocampal formation. Green and Arduini, observing a remarkably constant inverse relationship between hippocampal and neo-cortical electrical activity both at rest and on sensory stimulation, and finding that removal of the hippocampal formation alone produces surprisingly little change in behaviour, have suggested that the hippocampus exerts an inhibitory action on the posterior portion of the hypothalamus which, in its turn, is associated with visceral adjustments that take place in the transition between sleep and wakefulness and vice versa. This brings the hippocampus into relation with another great brain system—namely, the reticular substance of Moruzzi and Magoun. On the other hand, Green and Arduini have also suggested that the so-called theta rhythm described by Walter and Dovey in 1944, which has a bilateral temporal distribution in the electroencephalogram, is propagated through the hippocampal formation.

To return to the brain stem reticular system, Moruzzi and Magoun found that its stimulation caused replacement of the rhythm by low-voltage fast activity—*i.e.*, desynchronization of the cortical neurons—and this has since become known in electroencephalographic literature as the arousal reaction. The central reticular pathway, which includes tegmental nuclei, the subthalamus, the dorsal hypothalamus, and the intralaminar nuclei and reticular nucleus of the thalamus, is of vital importance in the maintenance of consciousness. Now in classical *petit mal* it is precisely this system that is interfered with. Jasper and Drooglever-Fortuyn were able to reproduce the three per second spike and wave phenomenon in all areas of the cortex by rhythmic stimulation of a small area (about two millimetres square) in the region of the *massa intermedia* and the intralaminar area, while Hunter and Jasper two years later, by rhythmic stimulation of moderate intensity of this area in unanæsthetized animals, produced the "arrest reaction", a phenomenon indistinguishable from clinical *petit mal*. It is interesting to note that Ingvar, repeating these experiments, was able to obtain this response from a much wider area than Jasper and Drooglever-Fortuyn, including the hippocampus and the cingular gyrus. This is important when we consider the clinical significance of the spike and wave phenomenon. I should like to discuss this in some detail, as there has been much confusion about it in the minds of clinicians.

Originally, E. L. and F. A. Gibbs described two types of wave and spike (to use the American form of the term) —the "petit mal discharge" (*i.e.*, three per second wave and spike) and the "petit mal variant" (*i.e.*, one and a half to two per second variety). As a number of subsequent authors have pointed out, it is undesirable to use clinical terms to describe electrophysiological phenomena, and there are many other varieties. Obviously the distribution as well as the wave form is important, and the Montreal school have stressed the importance of focal wave and spike as pointing to a cortical lesion. This aspect is amplified in a recent classification of Hill's, who divides the phenomena as follows: (i) Cortical spike and wave. This is confined to a definite cortical area without general spread. It is nearly always of the slow variety. (ii) Primary subcortical spike and wave, which may be of three types: (*a*) three per second spike and wave; (*b*) slow spike and wave; (*c*) fast spike and wave. (iii) Secondary subcortical spike and wave, which may be of the fast or slow variety; in these cases there is a spike focus in the temporal lobe, the medial surface or the orbital surfaces. For the sake of completeness we may add under the heading of primary subcortical spike and wave the polyspike and wave form often seen in myoclonic epilepsy, and an irregular spike and wave group. Here the irregularity refers both to the frequency of the slow wave and to the inconsistent appearance of the spike components. This last form is very frequent in children—it was present in 14·6% of the Maudsley Hospital series of epileptic children. Clinically this irregular spike and wave group differs from the classical three per second spike and wave group; the former have fewer *petit mal* attacks, more *grand mal*, and more seizures of other varieties—akinetic, psychomotor *etc.* I suggest that those cases are not examples of purely "highest level seizures", to use Penfield's term, and that something more than the centrencephalic system is involved, and I make a strong plea for the abandonment of the term "idiopathic epilepsy" in their case especially.

What is the present position regarding the significance of behaviour disorders in epileptic children? Here we meet the old organic versus psychogenic controversy with a vengeance. To give you a bird's eye view of the whole field, I should like to draw your attention to Strotzka's scheme. Strotzka, surveying the literature in 1955, pointed out four schools of thought which had approximately national boundaries: (i) the German school, who believe that character and personality changes take place on an hereditary basis; (ii) the American school, who deny any personality change and consider epilepsy to be a psychosomatic entity (few American authors, however, would go as far as this); (iii) the British school, who consider that psychiatric syndromes arise out of particular varieties of epilepsy; (iv) an Austrian school (to whose viewpoint many American authors would subscribe), who hold that epileptic behaviour symptoms arise out of a variety of organic, and more commonly environmental, factors. I think we can dispense with schools (i) and (ii) and try to decide between the third and fourth viewpoints. As Strotzka states, the third theory is based on a split-up, the fourth on a synthesis. The trouble about the latter is that it takes no cognizance of the varieties of epilepsy, whereas the former does. Nevertheless, there are a number of useful contributions coming from school (iv) and I should like to draw your attention to some of them.

The classical work on childhood epilepsy is the text-book of Bridge, which summarizes twenty years' experience of the epilepsy clinic at the Johns Hopkins Hospital. The approach is multifactorial and Myerian: epilepsy is due to a number of factors—hereditary, factor of brain injury, physiological, personality and environmental—and he considers each of these in their turn. Bridge, unlike some psychoanalytical writers (school (ii)), would not concede that emotional factors could by themselves cause fits, though they might aggravate them. In only 22 out of 742 cases did emotional factors appear to be important in precipitating the first fit, and even in these other factors were present. When Bridge comes to rate his five factors on a five-point scale and then intercorrelates them, he finds a positive correlation of 0·79 between the personality and environmental factors. This is not surprising, and naturally suggests a causal relationship between the two. Bridge points out that the quality of the behaviour problems of epileptic children is no different from that of behaviour disorders of non-epileptic children. I think nearly everybody is in agreement with Bridge on that point. He also points out that the background of the disturbed epileptic children is very similar to that of other problem children. Grunberg, at the Maudsley Hospital, has confirmed this by a recent statistical study. He matched 50 epileptic children with behaviour disorders with 50 non-epileptic disturbed children (the latter group all having normal electroencephalograms) and studied their environmental factors and heredity. He considered the following items: (i) maternal attitude; (ii) paternal attitude; (iii) epilepsy, psychosis, neurosis or psychopathy in parent, siblings or parents' siblings; (iv) sibling rivalry; (v) marital disharmony; (vi) excessive restrictiveness; (vii) breaks and changes in the environment. In none of these was there any significant difference between the two groups. This suggests that epileptic children with behaviour problems

are subjected to the same sort of pressures as non-epileptic disturbed children.

The value of Bridge's book lies in the fact that it contains a wealth of data; but these data are set out in a loose, untidy way, and the author continually mixes phenomenology with etiology. There is no attempt to tie up any particular variety of epilepsy with any type of behaviour disorder.

A different approach, but one that still ignores the physiologically distinct varieties of childhood epilepsies, is that of Charles Bradley, who divides the symptoms into primary (or "organic") and secondary (or "reactive"). The primary symptoms are (i) erratic variability in mood and behaviour, (ii) hypermotility, (iii) irritability, (iv) short, oscillating attention span, and (v) selective difficulty in mathematics. Bridge would have considered only irritability as a primary symptom. The other primary symptoms of Bradley surely indicate brain damage, without having any particular localizing value, and without having a specifically epileptic flavour. Hypermotility and short attention span are part of a syndrome which indicates diffuse damage, and which has been described by a number of authors, the account of Ounsted (1955) being a particularly good one. Next I should like to draw your attention to the work of Strotzka, the Viennese psychoanalyst. The writings of the Vienna school of Hoff and Strotzka seem motivated by a desire to minimize the importance of the Teutonic concept of the epileptic character change (*epileptische Wesens veränderung*). This state is not always described in the same way by every author, but it appears to contain two elements: (i) an "enechetic" element—stickiness, pedantry, circumstantiality, formalistic behaviour, forgetfulness and perseveration; (ii) an "explosive" element—irritability, aggressive outbursts, sometimes a general paranoid attitude. Naturally in children these features tend to be seen in a rather rudimentary form. Of a series of 256 epileptic children described by Spiel and Strotzka, this full-blown condition was seen in only 11 (4·3%). Strotzka and Werbenjak have discussed the mothers of epileptic children, and Navaratil and Strotzka made an interesting study comparing the attitudes of mothers of epileptics with those of mothers of children in day shelters. The attitudes they were interested in were rejection, guilt and over-protection in the Kannerian sense. The results showed much over-protection and guilt in the experimental group, but as the control group of mothers is a somewhat rejecting one I do not think that any firm conclusions can be drawn from their results. Nevertheless the findings are of interest, particularly to those who deal with mothers of epileptic children.

The approach to the parents is, I believe, of vital importance, and at the Maudsley Hospital the psychiatric social worker who deals with them has, over the years, formed some concepts which could be applied with profit elsewhere. To begin with, an explanation of epilepsy as electrical sensitivity is consoling as well as informative to the parents. Secondly, she discusses at length the parents' fear of the appearance of the fit—this arouses much more anxiety than the possibility of the child's hurting himself. Thirdly, she discusses the parents' fears concerning drugs, telling the parents their effects, and also goes into the questions of mental defect, criminal tendencies, inability to work, and invalidism, genetics, and school. Fourthly, she tells them how to use a gag if one is required, otherwise they may knock the child's teeth out or stick the point of a pencil into his cheek, and also gives advice regarding bicycles (generally they are not permitted), swimming, hard pillows for night fits, and job restrictions for adolescents dependent on the local labour rules. Fifthly, she gives a warning regarding over-protection of the patient and neglect of other children or of the parents themselves. Sixthly, she points out that the child with *petit mal* often has an over-strict conscience. Seventhly, she mentions the point that the child needs to be told about the fits, even though the parents swear that he does not know he has them. Last, she discusses any other psychological problems which the parents may cover up, as this is supposed to be a physical disease. We considered that in about half the families the child's epilepsy was the primary cause of intra-familial tension, whereas in the other half the fits merely served as a focus for more deep-seated abnormal interpersonal relations to graft themselves on. Naturally the management of the latter group needs to be much more prolonged and intense.

What are the environmental or psychopathological factors most relevant in the production of interictal conduct disorders in epileptic children? Grunberg, as part of the study already mentioned, attempted to find this out by matching 50 epileptic children without behaviour disorders with 50 children with behaviour disorders. The following factors were found: disturbed maternal attitude and breaks and changes in environment significantly different at the 0·1% level; marital disharmony and excessive restrictiveness at the 2% level. Unfortunately it could not be made clear from the data (which were obtained from the children's department item sheet) whether the disturbed maternal attitude was one of over-protection, over-solicitude or excessive hostility.

Finally, let us consider the third of Strotzka's four schools of thought—the one which, as you will recall, attempts to tie up the psychiatric picture with the clinical and physiological varieties of epilepsy. In the past ten years temporal lobe epilepsy has become fashionable, and there have been attempts to attribute any psychiatric condition in epileptics to temporal lobe involvement. This is the tendency among French authors, particularly those of the Marseilles school (Gastaut and his co-workers). An article by Paillas and Subirana points out that perseveration, the central feature or core of the so-called epileptic personality, is found in the Rorschach test of temporal lobe epileptics much more frequently than in the protocol of other epileptics. Among American pædiatricians Peterman makes a plea for the importance of temporal lobe epilepsy in the production of behaviour disturbances. He follows closely the arguments of F. A. Gibbs as applied to adults. Unfortunately, while recognizing the different varieties of childhood epilepsies, he makes no attempt to put any order into his behaviour data, and lumps together everything ranging from nervousness to being uncontrollable.

The peculiar character features of *petit mal* children were pointed out as long ago as 1906 by Friedman, who described them as "affectated and emotionally labile". He thought the attacks were hysterical phenomena, an error into which many clinicians have fallen since. This applies also to the interesting condition of *petit mal* status, in which the electroencephalogram (prolonged three per second spike and wave) can be somewhat of a revelation. Pond, in 1952, described *petit mal* children as having physical as well as psychological characteristics; the boys are fair and blue-eyed, the girls dark-haired and rather untidy-looking, and both sexes are serious, nice-mannered and rather passive, though they may be stubborn. The socio-economic status tends to be superior. In my quantitative behaviour studies I found that the true *petit mal* children were indeed remarkably unaggressive, less aggressive not only than the temporal lobe children but than all other physiological groups.

The same studies confirmed the fact that might be expected from experimental work on the rhinencephalon—that temporal lobe children were particularly aggressive, more so than any other group. It is an interesting fact that these children tended to come from a lower socio-economic group also. In this case it seems as if the environmental and the neurophysiological factors are working hand in glove to produce a particularly malignant picture. A small number of children (about eight) have had a temporal lobectomy; but the results are better considered in the larger context of the results of temporal lobectomy on the whole group of temporal lobe epileptics. Falconer and Pond wrote up three successful cases in 1953.

Other sub-varieties of childhood epilepsy are as follows: (i) The condition known as hypsarrhythmia or *Blitz-, Nick-* and *Salaamkrämpfe*, characterized by an early onset (generally before the age of five years). Most of the children are mentally retarded, and the course is downhill. (ii) Hyperkinesia with epilepsy. These are the most disturbed children one sees; the parents, according to Ounsted, show the condition of "excessive parental devo-

tion", and the family situation is generally a tragic one. (iii) Self-induced photogenic epilepsy. These children are generally passive, though obviously emotionally disturbed, and characteristically resemble ordinary *petit mal* children. They usually pose difficult psychotherapeutic problems, as anticonvulsants give disappointing results. Fortunately the condition is uncommon.

Conclusion.

To summarize, then, apart from intellectual defect, which is an extension of massive neurological deficit, there are three characteristic behaviour groups of epileptic children, the last of which is uncommon: (i) the timid, passive, intro-punitive, *petit mal* child presenting a neurotic picture; (ii) the aggressive temporal-lobe child, who acts out and shows the pattern which is generally called in child psychiatry a "primary behaviour disorder"; (iii) the extremely disturbed hyperkinetic child, who almost certainly has diffuse brain damage, which produces a marked defect in attention.

What about the rest—the children without temporal-cortical foci, the epileptics with normal and non-specifically abnormal electroencephalograms? These groups do not show anything specific in their behaviour patterns, and any type of psychiatric disorder may be seen in them.

Individual children may be very aggressive or very passive, but as groups they do not form characteristic patterns. There are as yet many cases in which we cannot be certain from the clinical and electroencephalographic data whether the rhinencephalic or the centrencephalic system, or both, or neither, is involved. Whatever the case, it seems to be necessary for abnormal environmental pressures to be present to initiate a behaviour disorder.

Having spent all this time in organizing the clinical and electrophysiological data, I have not said anything about treatment, apart from a few points in dealing with the parents. The truth is that the treatment of behaviour disorders in epileptic children is honest, down-to-earth child guidance. Whether this and the control of the seizures are carried out together at one clinic, as at the Maudsley Hospital, or at two separate clinics, as at the Royal Alexandra Hospital for Children, is a point of administrative convenience. Whatever happens, the psychiatrist should be aware of the electrophysiological data, and the pædiatric neurologist should have an idea of the environmental situation. They can thus combine in a rational approach to the child's condition as a whole.

I believe that the psychiatrist can contribute something to the problem of the epilepsies in childhood, but only if he has some grasp of neurophysiology, which provides the bridge that spans the gulf dividing the minds of the neurological and the psychiatric clinician.

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"ECOLID" IN THE TREATMENT OF HYPERTENSION.

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CHLORISONDAMINE CHLORIDE ("Ecolid") is a new ganglion-blocking agent discovered after systematic search for orally active hypotensive substances. Encouraging reports have appeared from the United States, the United Kingdom and New Zealand (Grimson *et alii*, 1955; Maxwell and Howie, 1955; Smirk and Hamilton, 1956).

We wish to report our observations on 15 hypertensive patients treated with this drug during the past eighteen months. These are not the results of a controlled trial,

but simply our clinical experiences at the Cardio-Vascular Clinic of Sydney Hospital.

Chemistry and Pharmacology.

Plummer *et alii* (1955), investigating a series of halogenated bisquaternary compounds, found that maximal ganglion-blocking potency and maximal oral absorption were associated with the interposition of only two carbon atoms between quaternary ammonium centres and with alkylation and quaternization by methyl groups. This led to the synthesis of "Ecolid", which is 4-5-6-7-tetrachloro-2(2-dimethyl aminoethyl)-isoindoline dimethochloride. Chemically, the most striking differences between this compound and the well-known ganglion-blocking agents hexamethonium and pentolinium are the presence of only two carbon atoms between the quaternary ammonium centres and the fact that one of them is in the form of an isoindoline ring structure.

The pharmacology of this new compound was studied in experimental animals by Plummer *et alii* (1955), by Trapold *et alii* (1955), and by Grimson *et alii* (1955). It behaved in all respects like a typical ganglion-blocking agent, affecting both the sympathetic and the parasympathetic system. Investigations in man by various authors, including ourselves, confirm these properties.

As with hexamethonium and pentolinium, the hypotensive effect of "Ecolid" is more pronounced when the subject is in the standing posture than when lying, and there is incomplete absorption when it is given by mouth. The ratio of oral to subcutaneous doses which produce similar effects has been found to lie between 7:1 and 28:1. When the effective dosage of the new compound was compared with that of pentolinium it was found that about half to nearly equal quantities of "Ecolid" are required for comparable hypotensive effects.

Subjects.

Fifteen patients, six females and nine males, have been treated with "Ecolid" over the past eighteen months. All but two of them (Cases XI and XIV), in whom there was possibly a renal cause for their disease, had essential hypertension; five (one with renal and four with essential hypertension) were in an accelerated malignant phase. The ages ranged from thirty-three to sixty-one years. Eight of the patients had previously been treated with ganglion-blocking agents, five of them satisfactorily. All had been under observation, even if not under active treatment, for some months before treatment with "Ecolid" was started.

All patients required active treatment according to the indications accepted by this clinic, which are as follows (Bauer, 1955): (*a*) accelerated or malignant hypertension with severe retinopathy (grade 3 or grade 4); (*b*) true hypertensive symptoms, especially those of left ventricular failure, paroxysmal nocturnal dyspnœa and recurrent pulmonary œdema; or (*c*) a rising diastolic pressure of 130 millimetres of mercury or more in young subjects, especially males. Some further details of the patients and of their response to treatment are shown in Table I. Eye-ground appearances are graded according to the classification of Keith, Wagener and Barker (1939), and electrocardiographic changes of left ventricular hypertrophy are graded from 0 to 3 according to our own classification based on the work of Sokolow and Lyon (1949) and of Scott *et alii* (1955). Blood pressure readings refer to casual pressures in the standing patient recorded to the nearest multiple of five millimetres, the diastolic pressure being taken at the point of disappearance of sound.

Technique of Treatment.

Patients were treated either as out-patients or as in-patients, without dietary restriction, and while continuing with any necessary drugs, such as digitalis. Other hypotensive drugs such as reserpine were not given in combination with "Ecolid". At the beginning of treatment, and then frequently, often daily, during the period of stabilization and occasionally thereafter, the blood pressure was recorded hourly throughout the day so as to judge the effectiveness of the morning dose of the drug. The dosage was increased and adjusted as necessary till a satisfactory response of blood pressure was obtained, unless side effects proved so troublesome that the dosage had to be reduced or administration of the drug discontinued.

Oral treatment was with 50-milligramme "Ecolid" tablets taken half an hour before or after food. The response in some individuals was more satisfactory when the drug was absorbed more rapidly from an empty stomach, whereas in others the delaying effect of food was an advantage. After preliminary experiences with the drug, our procedure was to give 25 mg. initially, once or twice daily, and then to increase the dose by 25 mg. each day or every second

TABLE I.

Case Number.	Patient's Sex and Age. (Years.)	Fundus Oculi Changes: Grade.	Electrocardiographic Changes: Grade.	Blood Urea Content. (Milligrammes per 100 Millilitres.)	Blood Pressure Before Treatment. (Systolic/Diastolic, Millimetres of Mercury.)	Treatment.			Blood Pressure During Treatment. (Systolic/Diastolic, (Millimetres of Mercury.)	Severity of Symptoms.[1]				Success or Failure.	Comment.
						Oral or Parenteral.	Daily Dose. (Milligrammes.)	Duration. (Days.)		H.	V.	B.	M.		
I	M.: 58	2	3	44	200/120	O.	150	17	130/100	1	1	2	1	S.	Insufficient supply of drug.
II	F.: 42	1	0	36	200/120	O.	200	4	150/90	0	1	0	0	S.	Insufficient supply of drug.
III	M.: 43	3	1	100	210/150	P.	2·5	14	140/100	0	2	0	1	S.	Rejected all treatment.
IV	F.: 54	2	3	34	210/120	O.	125	105	180/110	0	0	0	0	F.	
V (*a*)	M.: 53	4	3	85	240/140	O.	500	16	140/90	3	2	2	2	F.	
V (*b*)					210/120	O.	300	12	130/80	1	2	2	2	S.	Insufficient supply of drug.
VI	M.: 47	4	3	50	230/150	O.	300	5	160/100	3	3	3	2	F.	Rapid renal failure.
VII (*a*)	M.: 33	3	3	40	240/170	O.	250	19	180/130	2	2	2	0	F.	
VII (*b*)						P.	10	210	130/90	0	1	1	0	S.	
VIII (*a*)	M.: 44	4	3	26	280/190	P.	16	72	140/90	1	2	2	2	S.	
VIII (*b*)						O.	300	82	100/70	2	1	2	2	S.	Moved to country.
IX	F.: 42	3	2	25	240/140	O.	150	270	200/130	3	2	0	1	F.	Erratic response.
X	F.: 48	2	2	25	230/140	O.	125	350	160/120	0	1	0	0	S.	
XI (*a*)	F.: 61	3	1	40	260/130	O.	125	29	210/110	3	1	2	1	F.	Occasional severe effects.
XI (*b*)		4	1	40	260/150	P.	10	42	150/80	1	2	2	1	S.	
XII	M.: 55	2	1	26	180/130	O.	125	350	130/90	0	0	0	0	S.	
XIII	M.: 39	4	3	26	200/150	P.	14	120	150/100	0	2	0	1	S.	Died of renal failure.
XIV	M.: 54	2	1	22	250/160	O.	200	180	160/110	0	1	0	1	S.	
XV	F.: 45	1	0	20	220/140	P.	5	180	140/110	0	0	0	0	S.	

[1] Symptoms attributable to treatment are: "H", hypotensive; "V", visual; "B", bowel; "M", mouth.

day till a satisfactory response was obtained. An effective dose would lower the blood pressure maximally in about two hours, and would continue to affect it for six to twelve hours. Thirteen courses of oral treatment were given to 12 patients.

For parenteral treatment, "Ecolid" was supplied in one-millilitre ampoules containing five or ten milligrammes. Initially one milligramme was injected subcutaneously, morning and evening, and then the dose was gradually increased by increments of one milligramme. The effects of an adequate dose were noticeable within fifteen minutes, were maximal in one to two hours and persisted for six to twelve hours. Six courses of treatment were given to six patients. Patients learned to give their own injections with a tuberculin syringe, the regime being similar to that described for parenteral treatment with pentolinium. During treatment, patients were encouraged to maintain the upright posture in order to utilize the postural hypotensive effects of the drug. At night time patients were advised to sleep propped up on several pillows and with the head of the bed raised at least 12 inches.

The subjective effects of treatment, common to all forms of ganglion-blocking agents, were mainly symptoms of hypotension, photophobia and difficulty in accommodation, dryness of the mouth, and constipation. It is our practice to grade these according to severity: 0, no effect; 1, minor; 2, moderately distressing; 3, incapacitating or so severe as to necessitate a reduction in the dose of the drug.

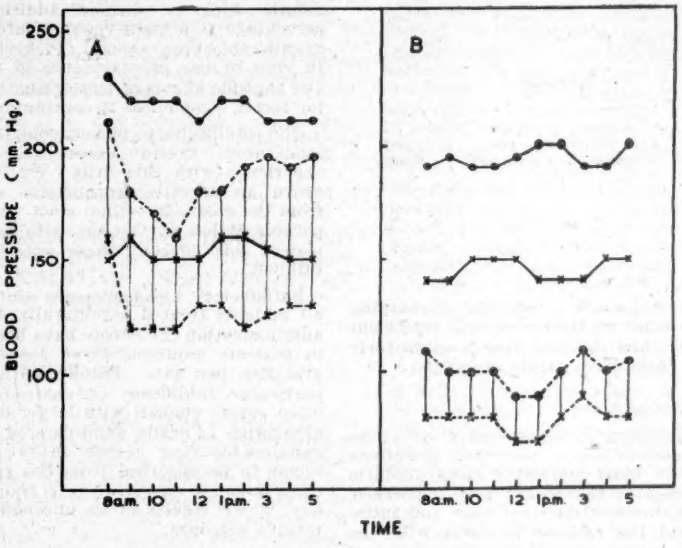

FIGURE I.

Blood pressures in two cases, recorded before treatment (continuous lines) and during treatment (interrupted lines) with "Ecolid" given at 8 a.m. Circles indicate the systolic and crosses the diastolic pressure.

Results.

Blood Pressure Control.

The blood pressure was reduced in all 19 trials of the drug. In most instances, but not all, postural effects were evident, similar to those experienced during treatment with other ganglion-blocking drugs. In two or three patients, however, "Ecolid" caused a fall in blood pressure which was no more evident when the patient was standing up than when he was lying down. Meals, exercise, alcohol, heat and mercurial diuretics accentuated the hypotensive effects, just as they do with pentolinium and other ganglioplegic drugs. Two examples of responses to "Ecolid" are shown in Figure I. The first shows a fairly prominent trough effect. The second shows a more uniformly sustained depression of blood pressure, which was only slightly influenced by posture. Some indication of the extent to which blood pressure was reduced in patients in the present series is given in Figure I, in which the blood pressure during treatment is the average trough level.

Treatment was apparently successful in 13 of the 19 trials. By success we mean that blood pressure was kept within reasonable limits, that severe eye-ground changes disappeared, and that true hypertensive symptoms were relieved, without undue distress from the effects of the treatment itself. In short, the initial indications calling for active treatment were tolerably controlled. All six of the parenteral trials were successful, whereas success was achieved in only seven of the 13 trials of oral treatment. Two of the patients taking parenteral treatment have continued with it for periods up to seven months. Three stopped, one after fourteen days because he was unwilling to continue with any form of therapy, two because they later changed for convenience, and with success, to oral treatment with "Ecolid" or mecamylamine, and one patient with severe accelerated hypertension died of renal failure after 120 days of treatment. The maximum parenteral dose required was 16 milligrammes a day. Of the seven patients successfully treated orally, three stopped treatment because of an insufficient supply of tablets at that time; three have continued for periods up to twelve months, taking daily amounts ranging from 125 to 200 milligrammes; and one reverted to the parenteral use of pentolinium because he moved to the country.

The incidence of side effects can be roughly gauged from the frequency of hypotensive and other untoward symptoms. One man taking tablets by mouth and one woman having injections noticed no ill-effects; three others on oral therapy and one on parenteral therapy had nothing more than minor symptoms. Visual disturbances (especially in the parenteral group), and constipation were the commonest complaints, as shown by the number of successfully treated patients who experienced moderately distressing (grade 2) symptoms (Table II).

Treatment was deemed to have failed in six trials of oral therapy. Two patients responded to treatment in the early stages, but later showed little or no response of blood pressure to a greatly increased dosage which caused excessively distressing side-effects. One of these (Case VII) reached a dosage of 250 milligrammes per day, and then changed to "Ecolid" by the parenteral route, by which his condition was successfully controlled. The other (Case IX) continued to take 150 milligrammes daily, but was inadequately controlled; it is proposed to change to treatment with mecamylamine. The other four patients suffered excessively from side-effects when control of blood pressure was anywhere near adequate.

The overall effectiveness of treatment in this series of cases, excluding those in which therapy was stopped solely because of lack of supplies, was as shown in Table III.

Hypotensive Crises.

The majority of patients experienced symptoms produced by hypotension at some stage or other. The trough effect usually produced by the drug was accentuated by a heavy meal, by exercise (especially on a warm day), by alcohol, by a warm atmosphere such as sitting before a fire, by prolonged standing and by any intercurrent infection. The effects were always corrected by lying down, and usually passed off within half an hour. Occasionally, however, some patients taking treatment by mouth had periods of hypotension at unexpected times, probably owing to vagaries

of absorption of the drug; in two instances they were severe and prolonged. One was a patient with severe hypertension in a malignant phase (Case VI) and moderately severe nitrogen retention, whose dosage was increased rather rapidly (when "Ecolid" was first made available to us) to 300 milligrammes on the fifth day. He developed profound hypotension which persisted for forty-eight hours. The other patient (Case VII), who subsequently failed to respond to a much larger dose and was changed over to parenteral therapy, experienced a similar crisis after a dose of only 50 milligrammes on the third day of his treatment. The attack lasted for thirty-six hours and was accompanied by abdominal pain and slight diarrhœa; it is possible that a mild attack of gastro-enteritis was the cause of this excessive sensitivity to the ganglion-blocking drug.

TABLE II.

Mode of Administration.	Symptoms.			
	Hypotension.	Visual Disturbances.	Bowel Disturbances.	Dry Mouth.
Oral (7 patients)	1	1	3	2
Parenteral (6 patients)	0	4	2	1

Irregularly occurring hypotensive attacks of varying severity were the main cause of failure of oral treatment with "Ecolid". However, when patients have been properly stabilized on treatment, these have rarely occurred.

Side-Effects.

Apart from symptoms caused by an excessive, or excessively rapid, fall in blood pressure, untoward symptoms produced by "Ecolid" were most commonly visual disturbance, constipation, dryness of the mouth and impotence, and less commonly drowsiness, abdominal pain and intestinal ileus. Some idea of the relative importance of the commoner side-effects is given by adding the grades of severity experienced by all patients—visual disturbance 26, constipation 20, dry mouth 17. Three patients noticed no side-effects at all. One was imperfectly controlled on 125 milligrammes daily, but of the others one showed a satisfactory response to oral treatment with 125 milligrammes per day maintained for twelve months, and the other to parenteral treatment with five milligrammes daily for six months. Several patients had only very minor symptoms.

TABLE III.

Route.	Success.	Failure.
Oral	4	6
Parenteral	6	0

Treatment was stopped or reduced to an ineffective level in seven patients taking "Ecolid" by mouth because of unduly distressing symptoms. These were mainly those due to hypotension—that is, to an exaggerated therapeutic response—rather than to side effects. Nevertheless, severe side effects were common among this group of therapeutic failures—rather more common, as might be expected, than among the successfully treated group. Moderately severe or incapacitating symptoms of hypotension were regularly experienced by six patients, visual disturbances by nine, bowel dysfunction by nine, and dry mouth by five. Few side effects were produced by oral dosages below 200 milligrammes per day; above 250 milligrammes per day, side effects were frequently distressing.

Visual symptoms could be partially corrected by using tinted glasses in bright light, positive lenses for close work and eserine drops. Constipation was overcome by taking liquid paraffin or by "Prostigmin" taken by mouth; in extreme cases the drug was omitted for one day.

Severe cramping pains in the upper part of the abdomen occurred in two patients (associated with a prolonged hypotensive crisis in one), and were thought possibly to have been caused by "Ecolid". Loose bowel actions were associated with the crisis and pains in one patient, and may have been due to another side effect of the drug.

Discussion.

In spite of the great advances during the past decade, the drug treatment of severe and accelerated hypertension remains a difficult problem. Whilst in some patients the condition can be controlled with pentolinium given by mouth, with or without additional reserpine, a large percentage at present require parenteral administration of ganglion-blocking agents (Pickering, 1955; Bauer, 1955). In view of the inconvenience of multiple daily injections and the side effects of parasympathetic blockade, the search for better compounds is continuing.

The preliminary pharmacological and clinical reports concerning "Ecolid" encouraged us to obtain first-hand experience with this drug. We had hoped that it would prove an effective hypotensive agent, reliably absorbed from the gastro-intestinal tract, and thus reproducing comparable action day by day with no, or minimal, pharmacological side effects. These expectations were only partly fulfilled.

Satisfactory blood pressure control has been achieved in all patients treated parenterally with "Ecolid". With oral administration the effects have been less reliable, especially in patients requiring large doses, in excess of 200 milligrammes per day. Parasympathetic side effects, and in particular inhibition of gastro-intestinal mobility, were often severe enough with larger doses to preclude uniform absorption of orally administered "Ecolid". As with other ganglion-blocking agents so far tested, only a fraction seems to be absorbed from the gastro-intestinal tract and thus becomes effective; this fraction varies from day to day, which results in an unpredictable and variable hypotensive response.

We therefore believe that, as with hexamethonium and pentolinium, "Ecolid" is better administered parenterally to severely hypertensive patients, unless adequate control can be demonstrated with a relatively low oral dose—that is, below 200 milligrammes per day. Our impression is that "Ecolid" is in some instances a better drug than pentolinium. We found the duration of action of "Ecolid" to be considerably longer than that of comparable doses of pentolinium, and have been able to control our patients satisfactorily on two injections per day, whereas they frequently required three injections of pentolinium. "Ecolid" is a valuable addition to the ganglion-blocking agents at present available for the treatment of severe and accelerated hypertension; but we are awaiting with interest our further experiences with yet newer drugs such as "Mecamylamine".

Summary.

Clinical experiences with a new ganglion-blocking agent "Ecolid" are reported. Fifteen patients have been treated for periods of up to twelve months. "Ecolid" was found to be a potent hypotensive agent capable of reducing blood pressure. The effect of the drug was more reliable and side effects were less troublesome when it was given parenterally than when it was given orally. The drug compares favourably with previously available ganglioplegic agents.

Acknowledgements.

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A NOTE ON THE OBSERVATIONS OF HEWSON AND FALCONAR ON THE MORPHOLOGY OF RED BLOOD CELLS, WITH AN ACCOUNT OF THEIR THEORY OF BLOOD FORMATION.

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Melbourne.

THERE are many simple everyday facts which we are apt to take for granted, forgetting that even the simplest of them were acquired only after a good deal of painstaking investigation, that they were often overlooked by the most brilliant investigators of the past, and that their discovery often had to wait upon developments in apparatus and technique. For example, every medical student today knows that red blood corpuscles are flattened biconcave disks. It is a fact that can be verified at any time by simple microscopic examination; and yet, from the time of Leeuwenhoek to the time of William Hewson (1739 to 1774), the "red particles" of mammalian blood were thought to be spherical. Hewson was assistant to William Hunter at the Great Windmill Street School and is famous for his work on the lymphatics and on blood coagulation. He and his associates, by means of an extremely simple modification in technique, took a distinct step forward when they were able to show that red blood corpuscles were discoid. However, they made two mistakes in their observations, in that they overlooked the fact that the cells were biconcave and they described the presence of a nucleus.

Their conclusions regarding the morphology of blood cells were the result of a series of experiments on human blood, and on the blood of other mammals, birds, amphibia, reptiles, fishes and invertebrates. Hewson died before the result of these experiments could be published, and their publication was left to a co-worker, Magnus Falconar. The latter repeated Hewson's experiments and published them in 1777 in a slim volume along with some anatomical studies of the lymphatics, thymus and spleen. On the basis of these observations, he enunciated a theory on the mode of origin of red blood cells. The title of Falconar's book was as follows:

> Experimental Inquiries: Part of the Third. Containing a Description of the Red Particles of the Blood in the Human Subject and other animals; with an Account of the Structure and Offices of the Lymphatic Glands, of the Thymus Gland and of the Spleen.
>
> Being
>
> The Remaining Part of the Observations and Experiments of the late Mr. William Hewson, F.R.S. and Teacher of Anatomy.
>
> By Magnus Falconar, Surgeon and Teacher of Anatomy.

This work was dedicated to "William Bromfield Esq., Surgeon to Her Majesty and to St. George's Hospital and to Percival Pott Esq., F.R.S. and Surgeon to St. Bartholomew's Hospital". In it the author gave entire credit to Hewson for initiating the experiments, and claimed only that he had repeated them himself. As the experiments and observations described in the book constitute a distinct, if slight, advance in our knowledge of the morphology of red blood cells, and as the theory that was advanced concerning their mode of formation is of historical interest, I propose here to give a brief account of the experiments and of the theory as set out in Falconar's book.

Blood Morphology.

The first chapter of the book dealt with the experiments carried out to show the true morphology of red blood cells. In a preamble to these experiments, it was stated that red particles had been seen not only in human blood, but in the blood of quadrupeds, reptiles, amphibia, birds and fishes, while similar globules, except that they were white in colour, had been seen in the blood of insects. In grasshoppers and caterpillars these globules had a greenish colour. Crustacea such as lobsters and shrimps, which also possessed white globules, were, following Linnæus, classified as insects. Examinations of the blood were carried out by means of simple microscopes made by London craftsmen. The strongest of these lenses was said to magnify up to 400 times and to have a focal distance of $^1/_{50}$. Father de la Torré, whose observations were frequently referred to, was said to have used lenses magnifying 640 and 1280 times, but his lenses lacked the clarity of those used by Hewson and Falconar.

Although Leeuwenhoek and others had seen that the red cells of amphibia were flat and elliptical, they had still believed that human and quadruped red blood cells were globular. Falconar thought this misconception was rather amazing, but attributed it to the great concentration of corpuscles in human and mammalian blood, which made the shape of individual corpuscles difficult to determine. However, he found that when human blood was diluted with serum so that individual cells could be distinguished, the discoid nature of the cells was readily apparent. It was also observed that they had a dark spot in the centre, and it was said that Father de la Torré had taken this spot for an aperture and, in consequence, had been led to believe that red corpuscles were annular. However, by careful examination they showed that this spot was not an aperture and therefore the particles were not annular.

In Plate 1 of his book Falconar showed sketches of the comparative shapes and sizes of the corpuscles of various animals as seen through a lens said to be of $^1/_{28}$ focal length. Three crucial experiments were made to prove these points about the morphology of red blood cells. The first experiment consisted of making a dilution of cells in serum and spreading it on a piece of thin glass. By placing the glass under the lens with a slight tilt so that the particles rolled downwards, it was possible to observe that some of the particles seemed to float on their sides, and, as they rolled over, it was quite obvious that they were flat. It was also noted that a few minutes after the blood cells had been spread out on the glass, they ran into clusters and stuck to each other. In other words, rouleaux formation was observed. From this it was deduced, firstly, that red blood cells are flat and not spherical, and secondly, that they are solid and not fluid, as had been commonly believed, because it was pointed out that any fluid, mixed with a larger quantity of another fluid in which it is insoluble, forms spherical and not flat globules. The manner in which oil forms globules when shaken up with water was cited as an example of this phenomenon.

The second experiment consisted of taking the blood of an animal with large blood cells, such as a frog, putting it on a glass, and adding water to it drop by drop. It was noted that when this was done the particle changed its shape from flat to spherical and finally dissolved. This experiment was repeated, using human blood. It was concluded that, since water made the particles globular and caused the dark spot at their centre to disappear, it

was evident that they were not perforated and that the dark spot was something other than an aperture. This was confirmed by the fact that if the spot was observed through a very clear lens, the middle part, which had appeared to be a dark spot when viewed through a blurred lens, was seen to be only a zone of a deeper red colour.

If the breaking up of blood cells was observed microscopically, it could often be seen to have fissured through the dark spot. There was no constancy about the number of pieces into which the corpuscle would break. This fact ruled out the popular theory that a red "globule" was composed of six "serous" ones.

It could be shown, too, that the cells were not of an oily nature, as had been suggested, for, as shown in the above experiment, they could readily be dissolved in water. To check this point further, the crassamentum was separated from the serum, and attempts were made to ignite each layer. If the red cells were oily they might be expected to ignite, but they failed to do so.

To answer the objection that, although the cells were flat outside the body, they still might be spherical within the circulation, the flow of blood was observed in the web of a frog's foot both with a solar microscope and with a simple lens. Under these conditions Falconar observed cells with their sides parallel and saw them turn over at the junction of two vessels. It had been said that the cells sometimes changed their shapes in passing through very small vessels. He thought this was because the observer who made this statement had seen them with their edges turned towards his eye. It was concluded therefore that red cells were flat within the circulation as well as outside it.

In the third experiment, the effects of strong solutions of various salts were observed. Shrinking of the cells and crenation, or "corrugation", as Falconar called it, were noted. He stated that, as a very strong solution of neutral salts and a very dilute one both altered the shape of the vesicles, it was probable that Nature had limited the proportion of water and salts in our blood. On cutting off the limb of a lobster and observing the flat vesicles in its tissue fluid, he noted that they became corrugated and formed irregular spheres on exposure to air. A similar observation was made by cutting off a shrimp's tail.

Theory of Blood Formation.

The anatomical features of the lymph glands, thymus and spleen were dealt with in Chapters II, III and IV respectively. Chapter V was devoted to a discussion of a theory of red-cell formation, which had been formulated from the results of the experiments and observations on the blood cells, lymphatics, thymus and spleen described in the previous chapters.

Falconar stated that the function of the lymphatics was the absorption of nutriments, but that they also assisted in forming red blood cells. The lymphatic glands secreted a fluid which, on microscopic examination, was seen to contain a number of small solid particles exactly resembling in size and shape the small dark particles contained in the vesicles of the blood. These particles that he observed in the lymphatic glands were, of course, lymphocytes. By means of the lymphatic vessels, these "central particles" were passed on to the thoracic duct and thence to the blood vessels. When we open a lymphatic vessel close to the gland, we find not only these "central particles", but also red blood cells completely formed. That is to say, we can see these "central particles" surrounded by a "vesicle". It was surmised from this fact either that the "vesicle" was a secretion from the internal coat, or that the lymphatic vessel had a "plastic" power of forming the vesicle from the contained fluid. The lymphatic vessel not only gave the corpuscle its "vesicle", but also gave it its red colour, because the central particle up to that point was white. In animals such as amphibia which have no lymphatic glands, it was thought that blood formation occurred in lymphatic networks.

It was also noted that the thymus gland was similar in structure to the lymphatic glands and secreted particles into the blood similar to those secreted by the lymphatic glands. It was thought to be large in the fœtus, because the need for blood production is greater in fœtal life than the lymphatic glands can handle. As the animal grows larger and the lymphatic system more extensive, it is able to handle the amount of blood production required without help from the thymus. The thymus gland is placed in the chest because the space it occupies there is not wanted during fœtal life. After birth, when respiration commences, the growth of the lungs demands that the cavity of the chest be enlarged. This was said to occur partly by the absorption of the thymus, but mainly by the growth of the structures constituting the chest wall. The spleen also was thought to "secrete" blood. The evidence given for this was, firstly, that if the spleen was diseased the body gradually wasted. Secondly, it had been proved that "central particles" were made by the lymphatic glands and thymus, and were conveyed into the circulation by the thoracic duct. They could be seen there if the blood was examined carefully. It was suggested that these were carried to the spleen. Here once again they could acquire their "vesicle" to become fully formed red blood cells.

Conclusion.

Some simple experiments are described by means of which Hewson and Falconar advanced our knowledge of red cell morphology. By diluting blood in serum and examining it with a simple microscope, they established the fact that red corpuscles are flattened disks. By treating the cells with water on the one hand and hypertonic solutions of various salts on the other, they observed the phenomena of hæmolysis and crenation. They also established the fact that the corpuscles were solid particles and were not globules of an oily liquid, and they proved that the dark spot seen at the centre of the cell was not a perforation.

But they made several errors in observation and in the theories they deduced from their observations. They failed to realize that the cells were biconcave, and that the "dark spot" was merely an optical expression of this fact. They mistook lymphocytes for "dark particles" identical with those at the centre of the red cell, and they failed to realize that red cells seen in the lymphatics occurred there by accident in the preparation of the specimen. As a result of these misconceptions, they postulated the erroneous theory that red cells were formed in the lymph glands, thymus and spleen, where they were built up from a central "dark particle" and a red "vesicular" portion derived from the walls of the lymphatic vessels.

All these errors can be attributed to the inadequacies of the simple microscopes used, and to the fact that the cells were observed without prior staining. Indeed, the fact that these workers observed as much as they did is remarkable, and reflects great credit not only on their own powers of observation, but on the skill of the craftsmen who made their lenses.

REVERSE TRANSFUSION.

By D. WRENCH AND J. C. A. DIQUE,
Brisbane Hospital, Brisbane.

THE fact that the blood flow in the superficial peripheral veins of the extremities can be reversed is not generally appreciated; yet this knowledge is of great practical interest during continuous intravenous therapy.

We ourselves made this discovery accidentally, whilst attempting to insert a canula into a superficial vein on the dorsum of the foot of a severely burnt patient, in whom all other superficial veins had been destroyed as a result of the widespread nature of his injury. When the vein had been exposed and tied distally, a cut was made proximal to the ligature, and it was noticed that blood flowed freely from the cut vein. In spite of this the canula was inserted with the tip directed proximally, but it was not possible to infuse any fluid; this was because the veins above the level of the incision had been

destroyed as a result of the burn. The canula was therefore withdrawn, the vein was tied proximally to the cut in it, and the canula was reintroduced with the tip directed towards the toes. Fluid flowed in readily, and it was possible to administer sufficient through this canula for the further treatment of this patient.

FIGURE I.

FIGURE II.

Since this incident, many patients of varying ages have been successfully treated by means of canulæ and needles which have been inserted with the points directed distally.

The following conditions may be regarded as indications for the insertion of the canula or needle with the point directed distally: (i) complete destruction of superficial veins of the limb after burning; (ii) the presence of tight dressings on the limb, as in skin grafting; (iii) phlebitis in the veins above the wrist or ankle; (iv) the presence of restraining bandages above the wrists or ankles in obstreperous patients.

FIGURE III.

FIGURE IV.

It appears that when the superficial veins of the forearms and legs are occluded or destroyed, the blood flow in the veins distal to the injury is reversed; the blood flows from the superficial veins to the deep veins by means of communicating branches, and this is possible because there are no functional valves in these regions.

In order to demonstrate the course of the blood flow venograms have been taken whenever it was not inconvenient to do so. Some of them are included here in a short account of the case to which each refers.

Reports of Cases.

CASE I.—A woman, aged fifty-five years, was admitted to hospital on January 31, 1957, for the relief of a strangulating small bowel obstruction. She was maintained on intravenous therapy for two days post-operatively, the needle point being directed distally (Figure I).

CASE II.—A man, aged sixty-seven years, had to be maintained on continuous intravenous therapy as a result of complications following gastrectomy for carcinoma of the stomach. During the rather worrying post-operative period he was given many transfusions, and on one of these occasions the needle was inserted in the reverse direction and a venogram was taken (Figure II).

CASE III.—An infant, aged one year, developed hypoalbuminæmia after gastro-enteritis and had to receive daily intravenous injections of 25% human albumin. The last injection was given with the needle in reverse, and a venogram was taken when the albumin had been injected (Figure III).

CASE IV.—A woman, aged fifty-two years, sustained a deep burn involving about 50% of the body surface, and extending over the thighs and buttocks. On her first admission to hospital a canula was inserted into the internal saphenous vein of the left leg in the usual way. The vein was left tied when the canula was subsequently removed. On a later occasion, after skin grafting a canula was inserted into the left foot, but with the point directed distally. On this occasion both her thighs and legs were firmly bandaged, and so were her hands, forearms and arms. The course of the blood flow can be clearly seen in the venogram (Figure IV), and also the site of the original ligature on the saphenous vein.

CASE V.—A man, aged seventy-two years, developed peritonitis after gastrectomy. He was maintained on intravenous infusions of four to five litres per day until he recovered. On the last occasion on which an infusion was given, the needle point was directed distally and a venogram was taken (Figure V).

CASE VI.—A woman, aged seventy-one years, developed a biliary fistula after exploration of the common bile duct, and was maintained on intravenous therapy for ten days before the fistula closed. The accompanying venogram (Figure VI) shows the course of the blood flow when the needle was directed distally. In this case the patient had some degree of phlebitis in the veins of the forearm resulting from previous infusions.

FIGURE V.

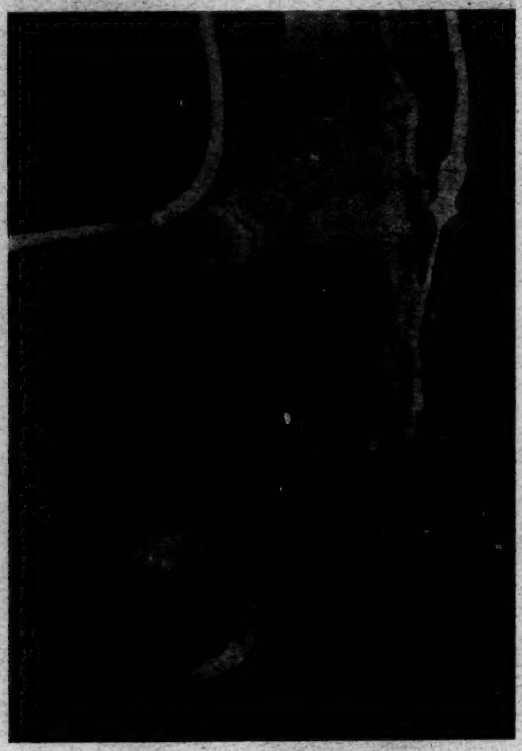

FIGURE VI.

Comment.

The rate of flow in these reverse intravenous transfusions has in all cases been equal to that of transfusions given in the usual way, and no difficulty has been experienced with blood or 25% human albumin.

This method opens up a completely new field for the intravenous introduction of fluids. It is offered as a useful manœuvre in cases in which intravenous fluid therapy has become difficult because of the shortage of veins.

Acknowledgements.

We wish to thank Dr. A. G. S. Cooper, Director of the Queensland Radium Institute, and his staff; Dr. P. A. Todd, the Director of Brisbane Hospital X-ray Department, and his staff for their cooperation in obtaining the venograms; and Dr. Frank H. Garlick and Dr. Keith Barnes for taking some of the films.

Reports of Cases.

ACUTE IDIOPATHIC ŒDEMA IN EARLY CHILDHOOD.

By E. P. SILBERSTEIN, M.B., M.R.C.P.,
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In children, gross peripheral œdema with ascites and pleural effusion is seen commonly in the nephrotic syndrome and in cardiac failure. Other causes of this symptom complex are very uncommon except in the newborn. When a child presents with massive œdema of fairly acute onset, one is therefore rather surprised if he does not either have albumin in his urine or present the features of cardiac failure. As these cases have rarely been recorded in the literature, one feels justified in presenting a single case.

Clinical Record.

A. had apparently been well until two days before his admission to hospital. He was aged one year and five months, was the first-born of an unmarried mother, and had spent all his life in a foundling home. Nothing abnormal is known concerning the medical history of the parents, except that his mother had spent some time in a mental hospital as a voluntary patient. The patient's development had been normal and his nutrition adequate. Two days before his admission to the Princess Margaret Hospital he was noticed to have some swelling of his eyelids, and this became more pronounced on the following day. He was examined by his own doctor, who gave him some antihistamine preparations. By the next morning his whole body had become swollen and he was sent to hospital. On his admission, the patient's appearance was like that of a child with a severe attack of nephrosis. His face was puffy and his eyelids were so grossly distended with fluid that he could not open his eyes. There was considerable pitting œdema of his lower extremities with moderate œdema of the trunk and upper limbs. There were bilateral pleural effusions and some crepitations scattered throughout the lung fields. The abdomen was grossly distended, chiefly because of the presence of ascites, and this made palpation difficult; but the liver was thought to be somewhat enlarged. There was no significant enlargement of the lymph nodes in his neck, axillæ and groins. The jugular venous pressure was not elevated, the heart was normal clinically and radiologically, and the pulse rate was 128 per minute. The blood pressure was recorded as 105 millimetres of mercury, systolic, and 65 millimetres, diastolic; but this figure is probably excessively high owing to difficulties in recording it in the presence of pitting œdema in a small child. It was later recorded as 80 millimetres of mercury, systolic, and 40 millimetres, diastolic. The temperature was 97·4° F. The urine contained no albumin, and no excess of white blood cells, red blood cells or casts. Details of the investigations are given in Table I.

Despite his extreme œdema and ascites, the patient never appeared to be really distressed. He was remarkably happy, even when he could hardly see because his eyes were closed by the palpebral swelling. He always took his feeds well and never presented any difficulties from the nursing angle. His treatment consisted of bed rest and a diet of low salt content (two grammes per day) and high protein diet content (85 grammes per day). His œdema disappeared in five days, during which period he lost five pounds in weight. As his abdomen became less distended and easier to palpate, his liver and spleen were found to be considerably enlarged. Both were firm, smooth and non-tender. Four weeks elapsed before they returned to their normal size. The course of the patient's illness while in hospital was one of rapid improvement, except for a transient respiratory infection which developed four days after his admission. In view of the patient's pleural effusions and the presence of penicillin-resistant staphylococci in the ward, he was given a short course of tetracycline. No complications ensued, and the intercurrent infection merely lasted a few days. The child's urine was tested daily and was normal throughout. The plasma protein content, on his admission to hospital, was 4·1 grammes *per centum* (albumin 1·4, globulin 2·5 grammes *per centum*), and it took about four weeks for the levels to return to normal (Figure I). The electrophoretic pattern is very unusual (Table II), and we have been unable to find a similar one in the literature.

Three weeks after his discharge from hospital (that is, six weeks after the beginning of the first illness), the boy

TABLE I.

	First Admission (June 21, 1956).	Second Admission (July 31, 1956).	Third Admission (August 29, 1956).
Urine:			
Albumin	Nil.	Nil.	Nil.
Erythrocytes	Occasional.	Very occasional.	Occasional.
Leucocytes	Nil.	Nil.	Nil.
Casts	Nil.	Nil.	Nil.
Chromatography	——	Normal amino acid pattern.	——
Blood urea	20 milligrammes per 100 millilitres.	——	——
Plasma cholesterol	184 milligrammes per 100 millilitres.	——	——
Plasma electrolytes:			
Sodium	140·0 milliequivalents per litre.	——	——
Potassium	6·5 milliequivalents per litre.	——	——
Calcium	5·4 milliequivalents per litre.	——	——
Chloride	105·5 milliequivalents per litre.	——	——
Plasma proteins:			
Total	4·1 grammes *per centum*.	7·4 grammes *per centum*.	8·0 grammes *per centum*.
Albumin	1·4 grammes *per centum*.	3·7 grammes *per centum*.	3·0 grammes *per centum*.
Globulin	2·5 grammes *per centum*.	3·5 grammes *per centum*.	4·8 grammes *per centum*.
Liver function tests:			
Thymol turbidity	1 unit.	1 unit.	——
Thymol flocculation	Nil.	Nil.	——
Serum bilirubin	0·5 milligrammes per 100 millilitres.	0·5 milligrammes per 100 millilitres.	——
Serum alkaline phosphatase	22 King-Armstrong units.	25 King-Armstrong units.	——
Hæmoglobin	12 grammes *per centum*.	12 grammes *per centum*.	11·5 grammes *per centum*.
White cell count:			
Total	8800 per cubic millimetre.	9400 per cubic millimetre.	8650 per cubic millimetre.
Neutrophile cells	72%.	28%.	43%.
Eosinophile cells	——	2%.	4%.
Lymphocytes	28%.	64%.	47%.
Monocytes	——	6%.	6%.
L.E. cell phenomenon	——	Not demonstrated.	——
Erythrocyte sedimentation rate (Westergren)	26 millimetres in first hour.	34 millimetres in first hour.	——
Mantoux test	Negative response.	Negative response.	——
Wassermann test	Negative response.	Negative response.	——

was readmitted with lobar pneumonia, which cleared up completely on a week's course of penicillin. The serum protein levels were again abnormal, with a decrease in the albumin content to 3·7 grammes *per centum*, and an increase in the globulin fraction to 3·5 grammes *per centum*. Electrophoresis again revealed a considerable increase in α_2 globulin content. The serum protein levels were still abnormal after the patient had been one week in hospital and was otherwise well; but they had returned to normal after a further week. Liver function tests were repeated and the results were found to be normal. The urine was also tested repeatedly; it did not contain any albumin or excessive quantities of aminoacids as shown by chromatography, and no increase of cells was found on microscopic examination.

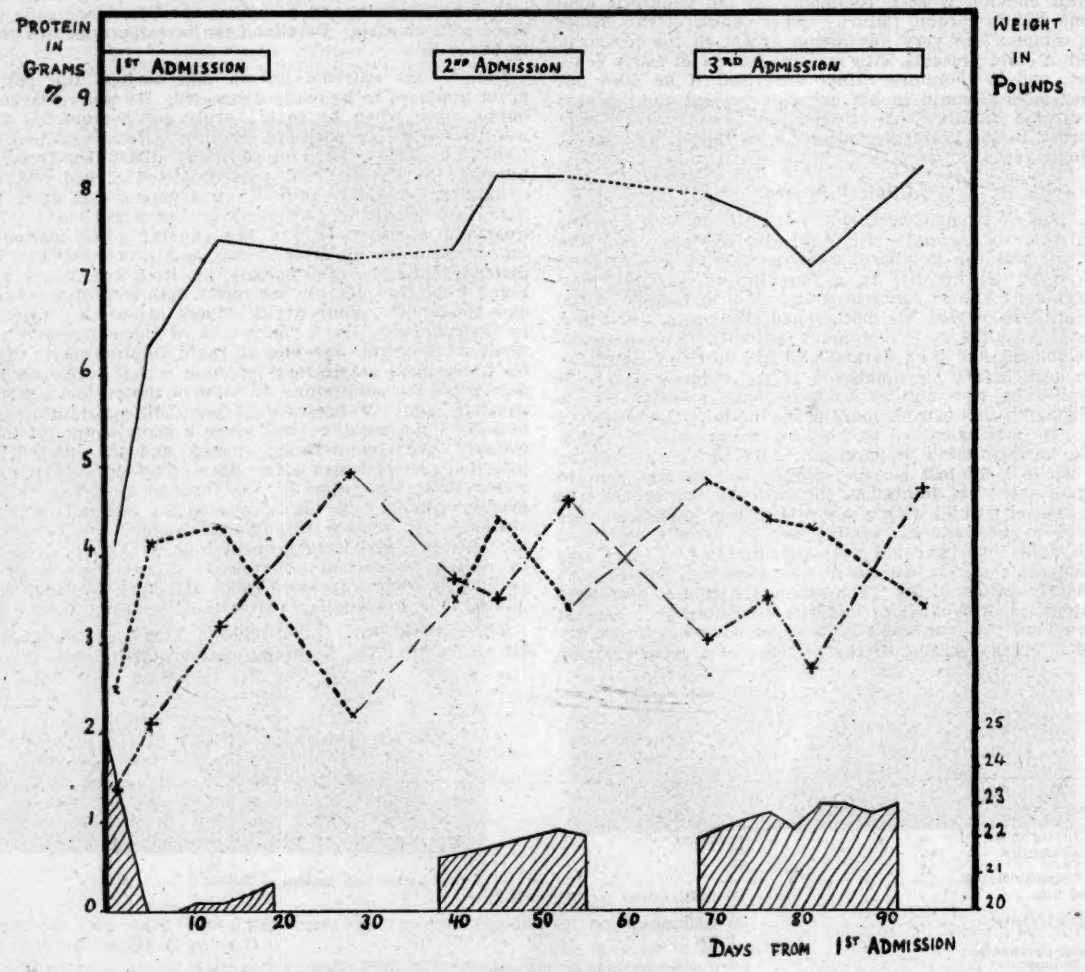

FIGURE I.

Solid line, total plasma protein content; dots and dashes, serum albumin content; dashes, serum globulin content; hatched areas, weight.

Two weeks later (that is, ten weeks after the beginning of the first illness) he was readmitted to hospital with acute suppurative *otitis media*. This was treated with ear toilets and penicillin, and settled down in two weeks. His spleen was again enlarged, the plasma protein level was eight grammes *per centum* (albumin 3·0 grammes *per centum*, globulin, 4·8 grammes *per centum*). The urine was again normal in composition and amount. The plasma protein levels and the spleen took about four weeks to return to normal.

During the past three months he has been perfectly well.

Discussion.

The principal features of the boy's illness are the sudden development of anasarca associated with a low serum albumin level and an enlarged liver and spleen. The disappearance of the œdema was almost as fast as its accumulation, and preceded by several weeks the return to normal of the serum albumin concentration and the electrophoretic pattern of the serum proteins. It is, of course, not unusual for the œdema fluid to disappear before the serum albumin level returns to normal, and this may be seen in nephrosis and cirrhosis of the liver. This is proof that the accumulation and disappearance of œdema fluid in these diseases is not simply a function of the concentration of serum albumin, and that factors such as the pituitary and adrenal hormones, renal function and capillary permeability may play some part. Estimations of antidiuretic hormone and adrenocortical steroids were not made in this case. In view of the persistent normality

TABLE II.
Findings on Electrophoresis.[1]

Electrolyte.	June 26, 1956.	July 4, 1956.	August 2, 1956.	August 16, 1956.	September 7, 1956.	September 25, 1956.
Albumin	−	±	±	N	N	N
α_1 globulin	++	++	N	N	N	N
α_2 globulin	+++	++	+++	N	+	N
β globulin	N	N	N	N	N	N
γ globulin	+	++	+	N	+	N

[1] "−", decreased; "±", slightly decreased; "N", normal; "+", slightly increased; "++", increased; "+++", grossly increased.

of the patient's urine and blood urea level, it seemed unlikely that there was any renal disease, and renal function tests were not performed. The capillary permeability was not grossly abnormal, as judged by Hess's test and the absence of purpuric manifestations.

The ætiology of this child's illness remains obscure. Nephrosis cannot be diagnosed in the absence of albuminuria. The child did not have any of the symptoms and signs of cardiac failure such as dyspnœa, raised venous pressure, triple rhythm or enlarged heart, and the enlarged liver was not tender. The child's nutrition had been adequate, the onset and disappearance of the œdema were far too fast for ordinary nutritional œdema, and gross œdema is not seen in beriberi in the absence of cardiac failure. I have never seen angioneurotic œdema which gave rise to such generalized œdema, to hepatosplenomegaly and to the serum protein disturbances described here. Serum sickness is excluded, as the patient had had no injections and his illness was not associated with fever. The child was far too well for the œdema to have been a manifestation of toxæmia.

Cases of acute generalized œdema with hypoproteinæmia were described by Meyer-Bisch (1925) and by Illingworth and Finch (1954). Meyer-Bisch's patients were probably adults, though that is not stated in his paper. The patients developed œdema suddenly, and this disappeared rapidly when they were treated with bed rest and a diet of low salt content. There was apparently no hepatosplenomegaly. Investigation showed that the patients had a low serum albumin level (the globulin level is not recorded) and a normal serum electrolyte pattern, but that they tended to retain sodium excessively when they were given a large amount of salt by mouth. Two of his patients also had signs of polyglandular dysfunction. In the two cases of Illingworth and Finch the œdema was of somewhat longer duration, and the hypoproteinæmia was associated with a low serum globulin level; also there was no hepatosplenomegaly.

Fever, generalized œdema and hypertension lasting but a few days and unassociated with abnormal urinary findings, but following upper respiratory tract infection with or without scarlet fever, have been described in the literature (Ferrini, 1872; Nonnenbruch, 1916; Kiglin, 1922; all quoted by Crofton and Truelove, 1948; Brod, 1949). The cases were thought to have been examples of nephritis, and some of these patients who died were found to have renal changes characteristic of acute glomerulonephritis. Unlike our patients, most of these patients were rather ill, they had no hepatosplenomegaly and hypoproteinæmia was not recorded; but the serum protein contents were not estimated in all the cases.

Cases of idiopathic hypoproteinæmia associated with œdema have been described by Wyngaarden *et alii* (1952), by Cope and Goadsby (1935), by Binger and Keith (1937), by Schick and Greenbaum (1945), by Hertzog and Faust (1950), and by Illingworth and Finch (1954). In these cases the œdema developed and disappeared far more slowly. Also the hypoproteinæmia in these patients was associated with a low globulin fraction and usually a normal albumin-globulin ratio. In one of Binger and Keith's cases there was evidence of liver disease.

Anasarca associated with atrophic changes in the liver was reported by Thompson *et alii* (1936). The œdema in their case accumulated rather more slowly, and did not resolve spontaneously or respond to a protein-rich diet. Also the serum globulin fraction was reduced almost as much as the albumin fraction.

It may be gathered from this survey of the literature that I have been unable to find a strictly comparable case recorded. It is possible that some cases recorded by Meyer-Bisch, Brod and Illingworth could be grouped with this case. However, hepatosplenomegaly was not detected in any of these patients, but this is possibly not a constant feature. The serum protein levels were not determined in Brod's cases, and Illingworth's patients had a low serum globulin as well as albumin level. From the investigations carried out it is impossible to be certain what the underlying disturbance was. Renal and liver biopsy may have thrown some light on ætiology, but these procedures were hardly justified in a patient who was recovering spontaneously at a rapid rate. It may be argued that the renewed plasma protein disturbance during the patient's attack of pneumonia and *otitis media* and the presence of hepatosplenomegaly suggest a developmental or acquired disease of the liver or reticuloendothelial system. Such a theory is not supported by liver function tests, but unfortunately these are not very reliable at an age of eighteen months. Hormonal functions may have been at fault, but unfortunately we had no facilities for estimating the concentrations of antidiuretic hormone, ACTH and adrenocortical hormones other than neutral 17-ketosteroids. Meyer-Bisch interpreted his cases as being due to a disturbance of electrolyte metabolism; but this could not account for the hepatosplenomegaly and the reversed albumin-globulin ratio. Whether capillary permeability was abnormal it is impossible to state, except that the glomerular capillaries did not allow of the filtration of plasma proteins, and that the skin capillaries were not permeable to red blood corpuscles.

Summary.

A case of acute generalized œdema of short duration, associated with hypoproteinæmia with reversed albumin-globulin ratio and hepatosplenomegaly of rather longer duration, is described and discussed. The disease seems to have a good prognosis. A study of the literature suggests that this may be a new disease.

Acknowledgements.

I would like to thank Dr. W. Seed, under whose care this child was admitted to hospital, for permission to publish this case. Thanks are also due to the laboratory staff at the Princess Margaret Hospital and the Royal Perth Hospital for the many investigations carried out.

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Reviews.

Dynamics of Psychotherapy: The Psychology of Personality Change: Volume 2. By Percival M. Symonds, Ph.D.; 1957. New York and London: Grune and Stratton. 9" × 6", pp. 269. Price: $6.50.

IN this second volume in his trilogy on "Dynamics of Psychotherapy", Professor Symonds discusses the process, with special reference to transference, resistance, abreaction, insight and identification. The patient benefits by psychotherapy only to the extent to which he undergoes a special emotional experience in transference, as described by Freud. But, following K. Horney, Professor Symonds does not look on transference as a repetition of emotional responses made to others during infancy or early childhood only. The attitude of the therapist is, of course, of vital importance. He should find pleasure and satisfaction in listening to his patients. The author quotes a list of 16 indications that the therapist is anxious or on the defensive with his client. The therapist should have no unresolved needs or conflicts or "certain trends and forces in his own personality of which he is not aware", although the author concedes that the therapist may correct certain immaturities and prejudices in his make-up as they come to light in his dealings with his patients. Great importance is attached to abreaction, which is distinguished from catharsis, the former being a reaction in the process of therapy in which a traumatic situation is revived, while the latter is applied to the recall of memories with an accompanying emotional discharge. The distinction seems to be more academic than practical. Professor Symonds maintains that in abreaction the response should be verbal rather than by "acting out" if the full therapeutic effect is to be obtained.

The two volumes are based on an extensive review of the literature on almost exclusively psychoanalytical therapy. How far the principles and theories propounded by the author have been leavened by his own experience remains to be seen with the appearance of the third volume on procedure. In the United States there is a considerable demand for courses in psychotherapy in faculties other than medical, and Professor Symonds, who occupies a Chair of Education, has written a text which should prove of great value in preparation for a written examination. The practising psychiatrist will find the work useful for reference. The reader will at least be made aware of the infinite complexity of interpersonal relationships.

Cleft Lip and Palate. By W. G. Holdsworth, F.R.C.S. (Edin.), F.R.C.S. (Eng.); Second Edition; 1957. London: William Heinemann (Medical Books), Limited. 9¼" × 7½", pp. 200, with 146 illustrations. Price: 42s.

THE appearance of a second edition of Holdsworth's little book only six years after the first is a clear indication that it has already proved its value.

The section dealing with the development of the face has been completely rewritten by Professor R. J. Harrison, who holds that in the past the story of the embryological development of this region has been over-simplified. It is interesting to note that some doubt still exists regarding the details of development of the philtrum and the central part of the red mucosa of the upper lip.

The chapter dealing with hare-lip follows the same general pattern as in the first edition; it is obvious, however, that the author, who previously favoured the Barrett Brown method for unilateral hare-lip repair, has now given his allegiance to the Le Mesurier operation. The actual choice of technique employed by surgeons no doubt remains, as a rule, with the operation which they have performed many times, and with which they have achieved satisfactory results. However, it is certain that while the Le Mesurier operation allows the formation of a central Cupid's bow in the lip, the incisions are more intricate and the possibility of asymmetry is greater than with the Barrett Brown operation. Moreover, many surgeons of experience hold that the presence of a Cupid's bow in an otherwise well-repaired lip is of minor importance only.

While the black and white drawings describing the various techniques of hare-lip repair are in the main well done, their descriptive value would be enhanced if several of the more important ones were shown in colour.

The description of cleft palate surgery is virtually unchanged; all the standard operations are well described, and the diagrams showing nasal mucosa in red and the oral mucosa in green help greatly to simplify the text.

The section on secondary operations has been considerably elaborated to good advantage, although, with the trend to direct facial cleft patients to special centres for their treatment, many of the gross deformities which were frequently seen in the past are now fortunately disappearing from our ken. In his "after operation" photographs of secondary repair, the author would do well to cause the subject to refrain from the use of lipstick, which can easily mask residual defects.

An entirely new chapter on orthodontic treatment has been added; this makes interesting reading, and stresses the importance of close collaboration between the surgeon and the orthodontist as members of the team dealing with the overall problems of facial cleft repair.

In summary, the second edition of this work can be recommended to all those aspiring to higher surgical degrees, as well as to those who wish to concentrate on this interesting branch of surgery.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Cats", by Brian Vesey-Fitzgerald; 1957. Mitcham, Victoria: Penguin Books Proprietary, Limited. London: Wyman and Sons, Limited. 7" × 4¼", pp. 272, with 32 illustrations. Price: 7s. 6d.

A fully illustrated and comprehensive guide to domestic cats: their history, breeding, showing, training and general welfare.

"Atomic Radiation and Life", by Peter Alexander; 1957. Mitcham, Victoria: Penguin Books Proprietary, Limited. London: The Whitefriars Press, Limited. 7" × 4¼", pp. 272, with 44 illustrations. Price: 5s. 6d.

The author is a member of the staff of the Chester Beatty Research Institute of the Royal Cancer Hospital, London.

"Psychoanalysis and Psychotherapy: Developments in Theory, Technique and Training", by Franz Alexander, M.D.; 1957. London: George Allen and Unwin, Limited. 8½" × 5½", pp. 326. Price: 25s. (English).

A summary and evaluation of recent trends in "dynamically oriented psychotherapy".

"Expert Committee on Biological Standardization: Tenth Report"; World Health Organization Technical Report Series No. 127; 1957. Geneva: World Health Organization. 9½" × 6¼", pp. 36. Price: 1s. 9d. (English).

Deals with the establishment of international standards and units in the immunological and pharmacological fields.

"Role of Hospitals in Programmes of Community Health Protection: First Report of the Expert Committee on Organization of Medical Care"; World Health Organization Technical Report Series No. 122; 1957. Geneva: World Health Organization. 9½" × 6¼", pp. 36. Price: 1s. 9d. (English).

An examination of the hospital's role in the provision of health care, in training and in research.

The Medical Journal of Australia

SATURDAY, SEPTEMBER 21, 1957.

Mervyn Archdall.

The death of Dr. Mervyn Archdall on September 6, 1957, was announced in last week's Journal. It followed closely on his retirement from the Editorship of the Journal and his honouring by the Federal Council with the Gold Medal of the Association in Australia. He will be mourned throughout Australia.

An obituary will be published later, when time has allowed the contributions of his friends to be collected. Meantime, as a tribute, we publish here the address given at his funeral service in St. Augustine's Church of England, Neutral Bay, on September 10, by his successor in the editorial chair, Dr. Ronald Winton. Dr. Archdall, in his own remarkable way, had expressed his wishes about the music and other details for this service and had asked that Dr. Winton give the address. It is unusual for statements of a personal character, especially with the use of the first person singular, to appear in our editorial columns, but it is appropriate that this address should be published as it was given.

IT was the expressed wish of my old friend and chief, Mervyn Archdall, that I should speak at this service. Those of you who knew him well will understand the diffidence with which I approach the task. He hated humbug, he despised cheap rhetoric and unctuous platitudes, and he had a strong sense of the fitness of things, particularly on special occasions. I am sure that he would have regarded this as a special occasion, and I feel a deep obligation to say what he would have considered fitting. Added to this, my own real affection for him makes the task doubly hard, as I may not be able to see his complex character as objectively as I would wish. For his was a complex and quite individual character.

From time to time a man or woman grows up amongst us who stands separate from the main group—an individualist, for good or ill. Such a person tends to be a failure or a success. He seldom remains in the rut of mediocrity with the bulk of us. If he is a success, he may achieve wealth or power or fame, again for good or ill. If, however, he has sincerity, honesty and goodness in his heart—and perhaps only then—he may become truly great.

This quality of greatness I believe Mervyn Archdall had. He was certainly not faultless. He would have been the last to suggest that he was, and I should be false to his memory to depict him so. In some ways he was a paradox. Like many great men, he could at times hold determinedly to a point that others thought trivial. Yet he more often saw things on the grand scale. Moreover, he could dream great dreams and then set to and bring the dreams to reality. Many people thought of him as austere and serious, and so he could be. Yet he had a tremendous sense of humour, a love of nonsense and the mischievousness of a small boy. He was truly liberal in spirit, and a thirst for essential truth took him along many paths—so much so that some once put him down as "pink" in his political philosophy. Yet no one more truly conservative could be imagined. He was impatient, as anyone found out who drove with him in his car in city traffic. Yet he lent a sympathetic and understanding ear to many a lengthy tale of woe. He was quick-tempered and strongly assertive of his own point of view at times. Yet he could be completely humble and self-critical, and he did many hidden kindnesses. These and other widely diverse strands went to weave the character that many of us loved. Enriching them were his great love of music, his breadth of reading and thought, his fierce demand for the truth and his faith in the things that are not seen.

In the 35 years of his association with THE MEDICAL JOURNAL OF AUSTRALIA, and especially in his 27 years as Editor, Mervyn Archdall served medicine and the medical profession with a single eye. Ill health dogged him all his life, but could not stop him before his appointed time. Indeed there was a fine and rare sense of completeness about his life at the end. On Saturday, August 31, he retired officially from the editorship of the Journal, knowing, as we all knew, that it was not in his nature to retire in fact. On the next day, Sunday, the Federal Council of the British Medical Association awarded him the Gold Medal of the Association in Australia—the one thing that he really valued and looked for amongst this world's honours, although only very few of us knew of this desire that he had. On Tuesday, the last time that I saw him, with a handclasp, a smile and a few words that mean much to me, he handed on the editorial torch that he had held so high. By Friday his last illness had moved swiftly to a climax, and he died in his sleep. He had finished what he had to do. Of his debt to his wife in the achievement of his greatness and in his last illness I will not try to speak, except to say that his debt was great and he acknowledged it in full.

For Mervyn Archdall medicine and its practice could not be divorced from loyalty to scientific truth or from service to man. In 1935 he wrote a sonnet on the death of a great friend, Eric Jeffrey, and published it anonymously in the Journal with Jeffrey's obituary notice.[1] It has remained anonymous at his wish, but I feel that now I may fittingly read it to you for what it tells us of the man who wrote it:

We greet you as you lie, unconquered, proud,
In peaceful slumber at the call of death,
And drape around you as a mystic shroud
The love and hope to which your life gave breath.
You came among us as a spirit clad
With radiant youth, with zest to love and live,
To toil, to thrill with laughter free and glad,
And treasures from your richest store to give.
Despite ill fate that sought with crushing blow
To quench the fire, to check your high emprise,
You did not falter. Rather did you grow
In courage and in strength. You bid us rise
Above the trammelled flesh and so to find
Our solace in the kingdom of the mind.

[1] M. J. AUSTRALIA, January 12, 1935, page 71.

But Mervyn Archdall knew an even greater realm than the kingdom of the mind, and the last thing that I must speak of is his faith. The son of a distinguished priest of the Church of England, he early learnt the Christian way. I think it is right to say that he never wholly lost sight of that background, though his quest for truth and his love for the adventures of living took him into distant fields. In his latter years he more and more desired rest for his restless spirit, and he looked in a more positive way towards the Christian verities. His heart turned gratefully to the greatness and mercy of God and to the redeeming work of Christ. He found a measure of peace for a spirit that could never be quite at rest in this world and he gained a growing confidence in what lay beyond death. At his own request this service is to close with the Hallelujah Chorus. He wanted no mournful farewell, no whimper at his end, but a shout of triumph—not because he had triumphed, but because he had confidence in the living God.

Current Comment.

CLAUDE BERNARD AND CURARE.

ON July 12, 1813, in the little village of Saint-Julien, near Villefranche, France, a boy was born. Like other small boys, he grew, and went to school. His early education was received at the Jesuit School of Villefranche, after which he proceeded to the college at Lyons. This he soon left, to become assistant in a druggist's shop. Following a not uncommon adolescent pattern, he occupied his leisure hours in writing, and produced a vaudeville comedy, which was so successful that he was led to attempt a prose drama in five acts. When he was 21 years old he went to Paris, armed with this play and an introduction to the critic Saint-Marc Girardin, who urged him to take up the study of medicine. This he did, in due course becoming an interne at the *Hôtel-Dieu*. From then on he went from success to success. The boy was Claude Bernard, and it is safe to say that his name will always be remembered in connexion with physiological study and research. When he died in Paris, on February 10, 1878, he was accorded a public funeral — an honour never before bestowed by France upon a man of science.

J. Bréhant[1] draws attention to the fact that, although curare has been in common use for the last fifteen years, very few mention the debt owed to Claude Bernard, who made the early discoveries on its physiological action. Bréhant urges all those who have not done so to read Bernard's "*Etudes physiologiques sur quelques poisons américains*", published in 1864. To judge by Bréhant's comments on the book, this advice could be taken with profit and pleasure, not only by medical practitioners, but by all interested in scientific detective work. There is no need to describe in detail the sinister ways in which certain tribes of South-American Indians used curare—this aspect of the subject is well known. However, when Claude Bernard came into the picture, the belief was widespread among explorers that animals killed by arrows poisoned with curare died painlessly, because they gave no signs of distress or agony. He was on the lookout for just such an agent "which dissociates and dissects the most delicate phenomena of the living organism". He believed that this poison would make it possible to separate the reflex arc into its constituent elements; it was intended to show that the physiological properties of the latter were organically entirely distinct. He injected curare into animals, and observed that after five or six minutes "they were dead, that is to say, respiration had ceased". In those words lies the whole spirit of the investigation — to show that it was not because the animals had ceased to breathe that they were dead; put another way, that death could not supervene except as a secondary result, after the animals had ceased to breathe for some time. Bernard sacrificed a number of animals immediately after their apparent death, and found that the heart was still beating, and that the blood became red in the air; by electrical stimulation, he found that muscle continued to contract when the stimulus was applied directly to it, but that there was absolutely no reaction when the stimulus was applied to the nerve. Thus the nerves were completely dead, whilst the other organic elements of the muscles, the blood and the mucous membrane were very much alive and retained their physiological properties for many hours. Here was proof that the sensorimotor arc could be broken, and that each of its elements was autonomous. The role of curare as a selective poison affecting motor conduction was revealed; all it did was paralyse, and it was only after the muscles of respiration had become affected in their turn that death supervened, by asphyxia. Claude Bernard described death from curare poisoning, that gentle death "which seems to us to occur so calmly and so painlessly", as being, on the contrary, "accompanied by the most appalling suffering that man's imagination can conceive", since the victim is helpless in the face of his spreading paralysis, and dies from suffocation without a single shiver that might betray his agony. Claude Bernard finally confirmed his findings by keeping alive, by artificial respiration, animals poisoned with curare until all the drug had been excreted in the urine; the neuromoter element thereupon revived and functioned again.

Curare has been tamed, and is now a regular and useful member of the anæsthetist's team of pharmacological assistants. Many workers have been involved in the long and difficult investigations that have led to this happy outcome. We do well to remember the pioneer work of Claude Bernard, who made the following prophecy: "Curare, like many other strong poisons, will certainly enter the domain of medicine."

[1] *Presse méd.*, 1957, 65 : 1047 (June 1).

THE OBSTRUCTED URETERO-PELVIC JUNCTION.

URINARY TRACT obstruction, dysfunction and infection are responsible for a large proportion of major urological problems—at least 90% of them, according to Robert Lich.[1] The most common site for supravesical congenital obstruction of the urinary tract is the uretero-pelvic junction. Lich points out that the prevalent concept of röntgenologists and urologists alike has been that uretero-pelvic obstruction is due to an extrinsic cause—*i.e.*, aberrant vessels, fibrous bands, *etc.* Actually, he states, these abnormalities are only rarely responsible. In view of repeated instances in which the resection of an apparently obstructing band or vessel was valueless in relieving uretero-pelvic obstruction, it became apparent that the cause of obstruction must be sought elsewhere. Furthermore, if one attempted to reconstruct the picture with the renal pelvis in its initial non-dilated state, the location of the obstructing band or vessel would seemingly be sufficiently far removed to be of no obstructive significance. After the pelvis became dilated, however, attendant alteration of the location of the uretero-pelvic junction could easily place it in an obstructive relationship to these nearby vessels or bands. The same situation can be visualized with reference to a high pelvic insertion of the ureter. In other words, as the renal pelvis enlarges, the uretero-pelvic junction is elevated until its usual dependent position is lost, and the picture of high insertion with apparent kinking results. Studies were made of the abnormal uretero-pelvic junction, and it was decided to investigate longitudinal sections of this area rather than the conventional cross-sections. With this change in technique, a consistent abnormality was found, which varied

[1] *Radiology*, 1957, 68 : 337 (March).

only in degree. In most instances of obstructed ureteropelvic junction there appeared valve-like structures that were always directed toward the renal pelvis, acting as an obstruction to the free flow of urine from the pelvis through the ureter, but seldom interfering with the retrograde passage of a ureteral catheter. Furthermore, the histological delicacy of these valves explains why antegrade instrumental calibration of the junction during surgery is not necessarily a measure of functional capacity. After observation of a considerable number of these patients, the normal uretero-pelvic junction was similarly studied and found to be free of valvular areas. Furthermore, in cases of moderately severe pyelectasis encountered at autopsy, valvular obstructions of varying degree were observed in the uretero-pelvic junction. It may be concluded that in most instances of pyelectasis the mechanism is a congenital intrinsic valvular obstruction of the uretero-pelvic junction, and that aberrant vessels or fibrous bands rarely play more than a contributory role. The method of surgical repair of the obstructed uretero-pelvic junction embodies the excision of the uretero-pelvic junction along with the redundant renal pelvis. A new uretero-pelvic junction is created by an anastomosis of the split ureter to the lower portion of the resected renal pelvis and closure of the remaining pelvis. The newly constructed uretero-pelvic junction is composed partially of ureter and pelvis, with an adequate lumen, and its construction is accomplished with technical ease.

AN UNUSUAL LOBOTOMY.

MANY and strange are the methods employed by would-be suicides, determined to find some way of leaving time and entering eternity. Surely one of the oddest is illustrated by the following case recorded by Jan Hryniewiecki.[1] The subject was a young man, aged 20 years, under treatment in a mental hospital for severe melancholic depression. In a moment of even more acute misery, he set about terminating his life by driving a nail into his head. His manner of proceeding was stoical in the extreme. He lay prone on a concrete floor with the nail (6·5 centimetres in length) held in his two hands. Then, using his head like a hammer, he hit it repeatedly on the concrete, lightly at first (like a carpenter would), then harder and harder, until he succeeded in driving the nail through his frotal bone and into his brain. The nail entered in the median line, penetrated the interlobular fissure and then entered laterally the left frontal lobe, coming to rest with its point in front of the *corpus callosum*. The man did not lose consciousness; he understood questions, but did not answer them. However, this mutism was in keeping with his mental state. He was able to obey simple orders. No neurological signs were found.

Twelve hours later the nail was removed by frontal trephining. The path of entry was carefully explored, hæmostasis was effected, and under antibiotic cover the *dura mater* was closed. There were no local complications. On the day after the operation, the patient suffered from slight psychomotor agitation. He was allowed out of bed 24 days later. It is sad to have to relate that his determined auto-lobotomy brought him no relief of his psychiatric condition; once more he took the path of the mental hospital.

"CLORPACTIN" IN INTERSTITIAL CYSTITIS.

INTERSTITIAL CYSTITIS causes much distress and is notoriously difficult to cure or even alleviate. It is therefore of interest to read a report by W. M. Wishard, M. H. Nourse and J. H. O. Mertz[2], of their experiments with a new preparation for local treatment, "Clorpactin". They were infected by the enthusiasm of V. J. O'Conor, of Chicago, for the use of this derivative of hypochlorous acid. "Clorpactin" (WCS 90) is a white, soluble powder, which is stable in the refrigerator, but which should be used within a few hours of being mixed with water. Chemically it is mono-oxychlorosene, whose active chlorine content is about 4%. It is most powerfully bactericidal, a 0·28% solution killing tetanus spores in five minutes. WCS 90 is the form of the drug most suitable for washing body cavities, renal pelves, fistulæ, wounds or the bladder cavity. It is highly buffered to a pH of 6·5. J. K. Lattimer reported in 1956 on its value in tuberculous ulceration of the bladder, while V. J. O'Conor reported in the same year on its use in interstitial cystitis. He used a 0·2% solution for very short periods (one minute) with over-distension of the bladder, repeating the treatment once weekly for about five weeks. The present authors dissolve 0·5 gramme in 250 cubic centimetres of distilled water. They avoid distension of the bladder, using only 30 to 60 cubic centimetres for one minute, after first cleansing the bladder gently with sterile water. This injection is repeated several times at a sitting, and the sittings are repeated once weekly for five treatments. Sedatives may have to be given afterwards to some patients. Twenty patients have been so treated, 18 being women; 14 patients obtained more relief than from any other previous method of treatment. However, cystoscopic control shows that the method does not effect a cure. Three failures were experienced, and in three other cases the improvement was slight.

[1] *Presse méd.*, 1957, 65: 842 (May 1).
[2] *J. Urol.*, March, 1957.

MACEWEN OF GLASGOW: THE STORY OF A SCOTTISH SURGEON.

THE name of Sir William Macewen has already found a secure place in the annals of modern surgery. It is, therefore, appropriate that an old friend in the person of Charles Duguid should help to complete the records with a small book of reminiscences as an intimate and sincere appreciation of his "chief".[1] This interesting biographical sketch is written by a Scotsman who came out to Australia many years ago to become a prominent surgeon in the city of Adelaide. He is able to write fluently and authoritatively of this great master of the craft from a close association extending over a period of several years at the beginning of this century. And the vivid impressions faithfully recorded here were obtained as a medical student in Glasgow, as Macewen's house surgeon at the Royal Infirmary, and as tutor in surgery and assistant to the Regius Professor at the University of Glasgow.

Although Macewen is said by some of his acquaintances to have been brusque in his manner, and inclined to be bluntly outspoken as a critic of immature scientific theses submitted for his scrutiny, he appears to have been possessed of many fine qualities which endeared him to his students and close associates in hospital and university work. He was undoubtedly outstanding as a teacher, clinician and surgical craftsman; in fact, he was "the acme of a scientific surgeon", patient, cautious, careful, and full of specialized knowledge in a variety of fields.

We are told that Macewen began his exploits in the new realm of neurosurgery in 1875, with a series of successful operations for brain abscess and subdural hæmatomata, and for the removal of tumours of the brain and spinal cord. Also, in 1895, he was the first to remove a lobe of the lung for tuberculosis, performing the operation with success on this and on subsequent occasions. He was an innovator in orthopædic work and devised his own methods in the use of bone-grafts. His story, as told by Charles Duguid, is one for all young surgeons to read and digest.

[1] "Macewen of Glasgow: A Recollection of the Chief", by Charles Duguid, M.A., M.B., Ch.B., F.R.F.P.S. (Glas.), F.R.A.C.S.; 1957. Edinburgh and London: Oliver and Boyd. 8½" × 5½", pp. 58. Price: 7s. 6d.

Abstracts from Medical Literature.

RADIOLOGY.

Mediastinal Carinal Bronchogenic Cysts.

J. G. DAVIS AND J. H. SIMONTON (*Radiology*, September, 1956) state that bronchogenic cysts are of congenital origin and originate in an abnormality in the development of the tracheo-bronchial tree. Mediastinal carinal bronchogenic cysts are located near or just beneath the bifurcation of the trachea. They are ovoid or round, homogenous in density, and usually well circumscribed. Rarely, they may show air-fluid levels if they have a bronchial communication. The shape may change with inspiration and expiration. In the postero-anterior view of the chest, the cyst is usually seen overlying the heart shadow and projecting more often to the right hilar area. In oblique and lateral views, it is usually posterior to the heart in the carinal region. The right and left main stem bronchi may be spread apart by the cyst. It may displace the œsophagus. Frequently it moves with coughing or swallowing. Dermoid cysts and teratomata are to be considered in the differential diagnosis. Usually these are in the anterior mediastinum, and they may be calcified. Thymomata also tend to occur in the anterior mediastinum, and are often lobulated. Lymphomata are as a rule lobulated and confined to the lymph node areas. An enlarged left auricle may give a similar appearance on the postero-anterior film. Bronchogenic cysts, however, are usually higher in location, and the characteristic posterior displacement of the œsophagus by the enlarged left auricle is usually absent. Aortic aneurysm may be suspected, but in the oblique and lateral views the cyst can usually be separated from the aorta. Angiocardiography will prove useful in such cases. Œsophageal and gastric cysts are similar to bronchogenic cysts, but are usually more posterior in location. Neurogenic tumours occur posteriorly and may produce erosion of either the spine or the ribs. A paraspinal abscess may simulate a bronchogenic cyst in the postero-anterior view, but lateral spine films will show vertebral destruction. Pericardial cysts are usually anterior in location and lower in position in the chest. Bronchogenic carcinomata, as a rule, are less sharply outlined than carinal cysts.

Lung Changes in Pertussis and Measles in Childhood.

J. FAWSITT AND H. E. PARRY (*Brit. J. Radiol.*, February, 1957) review the radiographic chest findings in 1894 cases of pertussis and measles occurring in children. In this series of cases there was found to be a preponderance of atelectasis in pertussis, and of hilar glandular enlargement and infiltration in measles. The percentages of bronchopneumonia and of pneumonic consolidation were approximately equal in the two diseases. The chest radiographs were considered clear in a higher proportion of the cases of pertussis than of measles. Children aged under one year showed fewer radiological changes than those aged over one year. The majority of deaths occurred in the younger age group. Residual chest changes on follow-up examinations were seen in approximately the same proportion of cases of pertussis as of measles, but the relative rarity of permanent pulmonary pathological change is stressed, and the evenness of its distribution between the two diseases is noted. In children with residual atelectasis the lung may take up to 10 or 11 months to reexpand.

Pathological Aspects of Mitral Stenosis.

J. E. EDWARDS (*Am. J. Roentgenol.*, October, 1956) states that the contribution of the radiologist to the clinical diagnosis of mitral valvular disease is made to a large extent by prediction as to the size of the left atrium. The subject of alterations in the position and contour of the œsophagus is not discussed, but the author presents the changes in the tracheo-bronchial tree that result from the enlarged left atrium. As the left atrium enlarges, its peculiar position with regard to the tracheal bifurcation results in an increased angulation between the two major bronchi. This increased angulation appears largely to result from the effects upon the left main bronchus. This is displaced upward, the result being an increase in the angle between the two bronchi as compared with the normal. Another phenomenon resulting from the upward enlargement of the left atrium and related to increase in angulation between the two bronchi is compression of the left main bronchus. Appreciation of the peculiar location and relation of the left main bronchus is necessary for understanding the factors leading to compression of it. The left atrium lies below. The left main pulmonary artery ascends in front of the left main bronchus and proceeds to a level above this, coursing behind the branch of the left bronchus, which goes to the upper lobe. In arching over the left bronchus, therefore, the left pulmonary artery tends to prevent the bronchus from rising, while the enlarged left atrium exerts forces in the opposite direction. This results in narrowing of the lumen of the bronchus associated with the formation of a sharp rather than a rounded posterior edge.

Ureteritis Cystica and Pyelitis Cystica.

B. S. LOITMAN AND H. CHIAT (*Radiology*, March, 1957) state that *pyelo-ureteritis cystica* is a benign and usually asymptomatic disease of the upper part of the urinary tract. Pathologically, it consists of small subepithelial cysts which elevate the mucous membrane of the renal pelvis and ureter and appear as round radiolucent areas in urographic studies. The lesions of *pyelo-ureteritis cystica* can occur at any point along the renal pelvis and ureter, but are most frequently found in the proximal third of the ureter. The typical pyelographic appearance is that of multiple small, round, lucent defects which cause a characteristic scalloping of the ureteral margins when seen in profile. The scalloping is produced by the projection of the submucosal cysts into the lumen, and represents an important differential feature of this disease. The cysts are usually scattered and discrete, but may occasionally cluster in small groups. They may be either unilateral or bilateral in distribution. Because of the frequent association of this disease with chronic inflammatory disease of the urinary tract, it is not surprising to find radiographic changes of both *pyelo-ureteritis cystica* and chronic pyelonephritis occurring concomitantly.

Radiological Manifestations of Psoriatic Arthritis.

T. F. MEANY AND R. A. HAYS (*Radiology*, March, 1957) state that psoriatic arthritis, as commonly understood, is a form of arthritis affecting patients with long-standing psoriasis. The joint manifestations predominantly involve the hands and usually are associated with psoriatic changes in the nails. The radiological findings in 15 cases of psoriasis and arthritis are grouped into two categories. The first group consists of rheumatoid arthritis, for which the term "psoriasis with rheumatoid arthritis" is used. In the second group the findings are not typical of rheumatoid arthritis, including varying degrees of articular destruction involving the terminal interphalangeal joints, which may progress to actual lysis of the joint and eventual fibrous or bony fusion. Depending upon the reaction of the patient to the disease, hypertrophic arthritic changes may be associated with these findings. Generalized demineralization of bone is not a feature of this second group. It is believed that the radiological changes found in the second group represent a distinct type of arthritis, for which the appropriate term is psoriatic arthritis.

Secretory Sialography in Diseases of the Major Salivary Glands.

P. RUBIN AND J. F. HOLT (*Am. J. Roentgenol.*, April, 1957) state that by correlative clinico-pathological and sialographic criteria, inflammatory diseases of the salivary glands may be classified in two groups, as follows. (i) Chronic obstructive sialodochiectasis, in which the abnormalities are primarily in the main duct. In this group, calculi and strictures are the principal pathogenic agents. Radiologically and histologically, the pathways which are dilated are the main duct and the interlobar and interlobular septal channels. (ii) Chronic non-obstructive sialodochiectasis or sialectasis, in which the abnormalities are principally in the peripheral ducts. This group is composed of heterogeneous but clinically related diseases which have a similar and characteristic pattern of "sialectasis". These entities include Mikulicz's disease, Sjögren's syndrome, and recurrent pyogenic parotitis in adults and children. With the utilization of the filling and emptying phases of secretory sialography, the altered anatomico-physiological pattern of sialectasis may be identified and classified into four stages: (*a*) punctate (early stage); (*b*) globular (moderately advanced stage); (*c*) cavitary (advanced stage); and (*d*) destructive

(end stage). The histological changes of non-obstructive sialodochiectasis common to the aforementioned diseases correlate with and confirm the radiological pattern of sparse, stenotic interlobar and interlobular ducts and dilated intralobular ducts. Secretory sialography is valuable in identifying tumours extrinsic to the salivary glands, since complete emptying of the duct system occurs immediately after stimulation of the glands to empty. However, intrinsic salivary gland neoplasms show retention of contrast material in post-evacuation films. Neoplasms of the salivary glands, from the radiological standpoint, are circumscribed or encapsulated and invasive. No attempt can be made to diagnose the histological type of neoplasm by sialography. The most consistent radiological finding in circumscribed or encapsulated intrinsic neoplasms is a filling defect outlined by a displaced duct system. The general architectural pattern of the duct system is preserved. Retention of contrast material in post-evacuation films is characterized by segmental intraglandular duct retention with differences due to the anatomical localization and size of the tumour. Infiltrative neoplasms characteristically show disruption of the gland architecture in the filling phase. The secretory phase shows retention of the contrast material where the acinar pattern is replaced by a bizarre puddling and pooling of the radio-opaque material. Correlation with the histological changes indicates that retention results because the normal acinar tissue has been destroyed or replaced by invasive neoplasm and the secretory function is lost.

The Radiological Diagnosis of Œsophageal Varices.

S. W. NELSON (*Am. J. Roentgenol.*, April, 1957) discusses the various factors of importance in demonstrating œsophageal and gastric varices. The author considers that if the following factors are kept in mind during the study of patients suspected of having œsophageal and gastric varices, the highest possible degree of diagnostic accuracy will be obtained. (i) Recumbent and Trendelenburg positions should be used. (ii) Thick barium mixtures are preferable, although various thinner mixtures will often suffice. (iii) Carboxymethylcellulose (0·25% to 0·75%) mixed with ordinary barium mixtures will improve the adherence of the barium to the œsophageal and gastric mucosa. (iv) Atropine sulphate in doses varying from 0·5 to 1·0 milligramme given subcutaneously 30 minutes before the examination, will also increase the adherency of the barium to the mucosa. (v) Multiple fluoroscopically controlled "spot" radiographs are necessary in varying positions, because smaller varices will often be shown in only one projection. (vi) Œsophageal peristalsis is very powerful, and a peristaltic wave can obliterate the varices. Under fluoroscopic control œsophageal relaxation can be observed and the radiograph taken of the œsophagus in a more relaxed state, during which the varices usually fill. (vii) The Valsalva manœuvre properly performed is usually of great value in demonstrating varices, probably because during the sustained Valsalva manœuvre (if the patient does not swallow) no further primary peristaltic waves are initiated and the œsophagus will eventually relax. (viii) Venous pressure will usually increase during the Valsalva manœuvre, and this, too, is thought to play a role in the visualization of the varices during this manœuvre. (ix) The phrenic ampulla, if present, can be of great value during the sustained Valsalva manœuvre, because the pinch-cock effect of the diaphragm can trap barium in the ampulla during the progression of the primary peristaltic wave towards the distal part of the œsophagus. If the Valsalva manœuvre is sustained, œsophageal relaxation will occur and allow small amounts of barium to flow backwards into the relaxing œsophagus; thus the varices will be demonstrated at an optimum time during their filling. (x) The Valsalva manœuvre will frequently prevent the visualization of varices in the lower part of the œsophagus, because the pinch-cock effect of the diaphragm during the manœuvre prevents filling of the varices from the abdomen. By discontinuing the manœuvre for three or four seconds, the varices may fill and then be properly photographed. (xi) In order to demonstrate varices in the abdominal portion of the œsophagus, respiration should be suspended comfortably in the expiratory phase. The Valsalva manœuvre will obliterate varices in the abdominal portion of the œsophagus. (xii) The Müller manœuvre will occasionally reveal varices when all other methods have failed. (xiii) Too much barium in the œsophageal lumen will frequently obscure even large varices. Relief techniques with the use of smaller amounts of barium are much more likely to be effective in demonstrating smaller varices.

RADIOTHERAPY.

Carcinoma of the Cervix Treated with Radiotherapy.

E. HARRISON (*Proc. Coll. Radiologists Australasia*, June, 1957), working at the Queensland Radium Institute, presents the results of 361 cases of carcinoma of the cervix treated between 1945 and 1950. All patients received intracavitary radium treatment, and most, except those with very early lesions, received deep X-ray therapy as well. The technique for radium insertion was the use of the Manchester method, 7000*r* being given to "point A", or 6500*r* in those cases in which deep X-ray therapy was given. This technique is discussed. Of 361 patients, 156 (43%) were alive and well five years or more from the time of treatment. Analysis by stages gave the following figures: Stage 0 (2 cases), 100% five-year survivals; Stage I (100 cases), 63%; Stage II (120 cases), 49%; Stage III (97 cases), 12%; Stage IV (24 cases), 4%.

The Mineral Content of Bone Tumours and Radiation Tumour Dose.

H. Q. WOODARD AND R. PHILLIPS (*Am. J. Roentgenol.*, July, 1957) state that the amount of radiation absorbed depends upon the chemical composition of tissue, and its distribution varies with wave-length. The authors have carried out precise measurements of both amount and distribution of mineral content in normal bone and in bone tumour in an attempt to assess radiation tumour dose. The actively-growing portions of primary bone sarcoma contain only small amounts of bone salts (not more than one-fifth or less than one-twentieth of normal bone). Secondary radiation from such bone salts is thus an insignificant fraction of total tumour dose, and therefore radiation quality is unimportant. In dense sclerotic tumour, however, damage to sarcomatous cells may be greater from medium voltage than from supervoltage rays; however, normal bone cortex has the largest calcium content, and therefore medium voltage will do more damage to normal osteoblasts than to sarcoma cells in so far as secondary radiation is concerned. The results indicate that the use of radiations of longer wave-lengths which are strongly absorbed by calcium will not appreciably add to tumour dose in irradiation of bone sarcomata. The use of rays of shorter wave-lengths (little absorbed by calcium) will do less damage to normal bone even if the same tumour dose is used.

Radiation Therapy in the Treatment of Retinoblastoma.

I. G. WILLIAMS (*Am. J. Roentgenol.*, May, 1957) discusses the pathology and prognosis in retinoblastoma disease and considers radiation therapy. He states that between 1934 and 1948 Stallard treated 15 children, using a radon seed technique; 14 are alive today. Since 1948 a new applicator has been designed, which is now loaded with ^{60}Co source. Up to 1955, 28 patients in whom one-third or less of the retina was involved have been treated with this radioactive cobalt disk, and 27 are apparently cured. Eight other patients have been treated by deep X-ray therapy followed by the application of ^{60}Co disks to the residue of the neoplasm. In all these, more than half the retina was involved. One has some vision, three are blind, and four have subsequently had the blind irradiated eye excised.

Radiotherapy of Non-Malignant Diseases of the Eye.

M. LEDERMAN (*Brit. J. Ophth.*, January, 1957) discusses the use of low voltage X-ray therapy and beta irradiation in non-neoplastic diseases and benign tumours. The aims are to relieve symptoms, to promote healing (*i.e.* by resolution of inflammatory process or absorption of hæmatoma *etc.*), to affect blood vessels, to reduce intraocular tension, and to restore function. The mode of action is not known, but possible mechanisms are stimulation of antibodies, and effects on cellular elements of exudate or on the blood vasculature. Of many conditions listed, the author considers the following of most importance to the radiotherapist: Mooren's ulcer, *rosacea keratitis*, corneal vascularization, virus infections, vernal catarrh and pterygium, and amongst the benign tumours, hæmangiomata, papillomata, keratoses and keloids. The author discusses factors influencing the choice of techniques of treatment, and presents results of treatment.

British Medical Association.

NEW SOUTH WALES BRANCH: SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on April 24, 1957, at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, DR. A. W. MORROW, the President-Elect, in the chair.

Epilepsy in Childhood.

DR. E. L. DAVIS read a paper entitled "Epilepsy in Childhood" (see page 420).

DR. E. J. A. NUFFIELD read a paper entitled "Interictal Events in Childhood Epilepsies: Their Psychiatric Significance" (see page 424).

DR. WILFRED CARY, in opening the discussion, said that epilepsy was of great importance and interest to all pædiatricians; over the last eight years he had taken a particular interest in it. The more he saw of it, the more he realized that the problem was not just that of controlling the convulsions with the right anticonvulsant. There were a number of interesting facets. First, there was the widely held view amongst the public, and certainly amongst many medical practitioners in New South Wales, that the epileptic child deteriorated intellectually, and that the majority of epileptic children were mentally backward. Pinter, in New York, had analysed a series of 200 epileptic children, and showed that the proportion of backward children amongst them was no greater than in a control group. Lennox held very strong views on that point. He thought that the backward children among epileptics could be divided into three categories: (i) a brain-damaged group; (ii) a group that he called genetically determined; (iii) a group showing pseudo-deterioration. Dr. Cary thought the third group was important; it was not recognized readily enough, and many of those epileptics were branded as mentally backward when they were nothing of the kind. Lennox stated that isolation from normal or stimulating contact, fear, shame and discouragement led to stagnation of thought closely resembling mental defect. Dr. Cary thought that there must be many epileptic children in the Australian community who had been labelled as mentally defective, but were suffering from just such a state. Another common cause of pseudo-deterioration in the Australian community was over-sedation. Over-sedated epileptic children were very common, and were easily labelled mentally defective by the unsympathetic medical practitioner or school-teacher. The importance of that group was that in it the condition was reversible, and should be reversed. Dr. Cary then posed the question whether severe and prolonged convulsions caused mental deterioration. That was what parents always asked, as they watched the horrifying attacks; and as the medical attendant watched them himself, and saw the children cyanosed sometimes for long periods, he also wondered about it. Lennox was definite in his views that any mental deterioration was based on preexisting brain damage, and that the convulsive processes themselves, no matter how prolonged they were or how much cyanosis they produced, caused no further deterioration. Dr. Cary said that he himself found that a little hard to accept; he asked for comments from the speakers.

Another facet of epilepsy in childhood important to the pædiatrician was the febrile convulsion and its relationship to epilepsy. In a given year, some 2% of admissions to the Royal Alexandra Hospital for Children were for febrile convulsions. That was much more than the admissions for rheumatic fever, tuberculosis or many of the illnesses that were regarded very seriously. Of course, many hundreds of children with febrile convulsions might never reach the hospital. At the Institute of Child Health, the problem was regarded seriously enough for a retrospective study to have been carried out some years previously. The records of 100 children who had been admitted to hospital for an attack of febrile convulsions were collected, and the children were followed retrospectively for ten to fifteen years. Of the 100, only six were thought to be epileptics after that period, which Dr. Cary realized was still a short period. The others had been completely normal for some years. It would therefore be agreed that febrile convulsions must be a benign illness in childhood. Referring to the ætiology of febrile convulsions, Dr. Cary said that his own opinion was that the community could be divided into roughly three groups. The first was a very large one, composed of such people as those present, who might be termed to have a very high epileptic threshold; but if they were given enough "Cardiazol" or insulin or electric shock, they could be made to have convulsions. At the other end of the scale was the epileptic, who seemed to need no overt stimulus to have convulsions. In between lay a group among whom were children who had febrile convulsions, who had a convulsive potential, quite a low threshold, but needed something to set them off. Such a stimulus could be a fever associated with tonsillitis, otitis or gastro-enteritis, or even appendicitis. The convulsions might even follow an emotional episode, such as a birthday party or some frustrating experience. Naturally, convulsions in such circumstances were commonest in the young child, whose nervous system was less well developed—the myelin was immature and there was more fluid in the central nervous system. As the nervous system became more mature, the child required a greater stimulus to have convulsions. Ultimately, as he had shown, 94 out of 100 became entirely normal. Dr. Cary went on to say that another very important facet of epilepsy in childhood, and a very common one, was the handling of severely epileptic children, most of whom had brain damage, and who showed backwardness and behaviour disorders and often hyperkinetic behaviour. It was all very well to talk about giving anticonvulsant drugs and stopping the convulsions; that was by far the easiest part of the treatment. The parents did not worry about the convulsions—they came to accept them. It was the rest of the treatment, as Dr. Nuffield had said, that was difficult; it took much understanding and sympathy, the cooperation of the child guidance clinic, the almoners and the social workers, and a great deal of hard work on the part of the pædiatric physician, to help such children, and to sort out their capacity to learn and to decide where they should be sent to school—in short, to determine just what could be made of them. Dr. Cary thought that extremely important in the handling of epilepsy in childhood, and it was almost entirely neglected in the Australian community.

Dr. Cary finally referred to the question of dosage. He said that commonly, when the practitioner was called in to see a child who was having convulsions, or who had had a series of convulsions, he began treatment with one-quarter of a grain of phenobarbital perhaps twice a day. That did not do much good. He was called back after a week or so, and perhaps he added half a grain of "Dilantin" twice a day. That might or might not help; but the child still had some convulsions, so the practitioner tended to regard the child as incapable of being relieved, and to say that the treatment he had received was all that modern science could offer. Dr. Cary said that it was his firm belief that, in treating convulsions in childhood, one should, after thoroughly examining the child and having an electroencephalogram taken, choose what one thought would be the most effective drug or combination of drugs, and start with a dosage that was likely to be effective. If it was not, one increased it until either the child ceased to have convulsions, or else he began to have symptoms of toxicity or some side-effect. If that happened, one changed to another drug. The important thing was to keep pushing the drug. Dr. Cary remembered one child at the seizure clinic at the Royal Alexandra Hospital for Children who had very severe *petit mal*. He gave no response to nine "Tridione" tablets; on ten his convulsions entirely stopped, and he had no side-effects.

DR. D. G. HAMILTON said that major seizures occurred commonly as a feature of genetic epilepsy in childhood. There was one form of fit common in childhood which had not received the mention that it deserved—the larval *grand mal*, or minor motor seizure as Bridges called it—the aborted major fit. Often a patient came with a letter stating that he suffered from *petit mal*; but a careful history revealed that it was certainly not *petit mal*. The term *petit mal* should be reserved for turns consisting of transient oblivion, with a three cycles per second spike and wave pattern in the electroencephalogram; but the children who had larval *grand mal* seizures had short seizures with some of the manifestations of major fits. The manifestations of major fits were clonus, tonus, cyanosis, post-ictal sleep and complete unconsciousness. The minor motor fit had some of those characteristics; the child might have only two or three clonic jerks; he might be clonic and cyanosed, and then sleep afterwards; the whole attack might take only thirty seconds, but it was not *petit mal*. It was minor motor epilepsy, because it had some of the characteristics of the major fit. Its treatment was not by the "dione" drugs, but by the drugs used for major seizures.

Dr. Hamilton said he was glad that so much had been said about the emotional impact of epilepsy on the child and on the parent. He thought it very true that practitioners

failed in their duty to the family if they failed to take that into account. Dr. Hamilton instanced a small girl who had three or four fits per week, and was excluded from school because of that. She was a child of normal intelligence, and at home was bored, unhappy, with little to do, frustrated. She became quite a "behaviour problem". Then she was enrolled in the handicapped children's school at the Royal Alexandra Hospital for Children, where she became a happy, occupied little girl, and with no other change in treatment the number of seizures dropped from three or four per week to one each three or four weeks. Dr. Hamilton was sure that the emotional tension that occurred in children made their epilepsy much worse. He was also sure that if practitioners would take time to inquire about the emotional pattern of epileptic children's families, they would find that among the parents there was often enormous stress, caused by their lack of understanding of the disease from which their child was suffering. Dr. Hamilton had been interested in what Dr. Nuffield had said about the discussion of the family problem with the parents by a social worker at the Maudsley Hospital. In Australia such luxuries were lacking in adequate amounts. Dr. Hamilton believed that doctors must do the work—they must find out from the parents of epileptic children all that the disease meant to them. On the question of restriction of swimming, Dr. Hamilton said that that was naturally among the restrictions placed on epileptic children. However, he had as a patient an epileptic boy who had *petit mal* seizures, and who was quite a champion swimmer and would not give it up. The boy's father said that on a number of occasions the boy had been in the water and had a *petit mal* seizure while he was swimming. His swimming would suddenly slacken off, some sort of rhythmic swimming movement continued for perhaps fifteen or twenty seconds, and then he picked up and continued his former stroking. Dr. Hamilton said that he had also seen a boy catching a ball, and have a *petit mal* seizure just as he caught it; he caught the ball, and during the fit went on with a slow, rhythmic throwing of it a few inches into the air and catching it again. When the fit stopped he continued with the game. In mild *petit mal* seizures it was interesting that activity in a somewhat modified form could go on. Dr. Hamilton emphasized the optimistic attitude that Dr. Cary had stressed in relation to epileptic children. He said the brain-damaged child with mental backwardness did present a grim picture. However, he believed that the majority of other epileptic children grew out of their epilepsy if they were properly treated, and he hoped that it did not recur later on in life. The pædiatrician's attitude to epilepsy should be essentially optimistic, and he should endeavour to educate the public into believing that it was not a grim and dreadful disease, but a treatable disease.

DR. CEDRIC SWANTON asked Dr. Nuffield what he thought about the psychological precipitating factors in stimulating self-induced photic epilepsy. Dr. Swanton said that he would like to support, very strongly, what Dr. Cary had said about the treatment of major epilepsy with "Dilantin", up to the patient's maximum tolerance, if the fits were not controlled, even to the production of ataxia or diplopia before other drugs such as barbiturates *etc.* were added to the therapy. In support of this, Dr. Swanton quoted the case of a child, aged two and a half years, whom he had seen with the late Dr. Edgar Stephen. The child had been having frequent fits for the previous eighteen months, and had gone into *status epilepticus*; chloroform was being given in an attempt to control it. It was suggested that the child be given a large dose of paraldehyde *per rectum*, and the child came out of the *status epilepticus*. "Dilantin" had only just become available, and Dr. Swanton suggested that the child be put on a dosage of four half-grains per day. He did not see the child for ten days; he was then called again, because the child was diplopic and ataxic to the extent that he could not stand or walk and that he could not find his mouth with his hand and so on. It was then discovered that the child had been gievn four one-and-a-half-grain capsules of "Dilantin" instead of four half-grain capsules; in other words, that very small child had been having six grains of "Dilantin" per day. The child was then placed on a maintenance dose of half a grain three times a day, which was continued for the next three years. The child had never had a fit subsequently, and had now matriculated and was doing a university course. In view of that, Dr. Swanton said that he had, at times, put a patient with major fits, who was difficult to control, into hospital, deliberately intoxicated him with "Dilantin" until his fits ceased, and then put him on a maintenance dose. Dr. Swanton agreed with Dr. Cary that it was not good practice merely to put a patient on "Dilantin", one and a half grains three times a day, with perhaps phenobarbital or "Prominal" twice a day, and be content with merely diminishing the number and frequency of the fits.

Dr. Nuffield, in reply to Dr. Swanton, said that it was difficult to generalize from the three cases of the condition that he had encountered. The psychological stimulating factors seemed to be varied. What had struck him about the affected children was their general personality; often they were aged about twelve to fourteen years, they were all in great conflict with their parents (particularly their fathers), and any expression of resentment which they allowed themselves seemed to produce that phenomenon. He supposed that inability to express resentment, and any expression of resentment, led to self-stimulation. It could be deduced from that that the condition was a form of self-punishment.

DR. ROSS WILLIAMS asked Dr. Davis and Dr. Nuffield whether they had had any experience of the type of child who developed a behaviour problem after the convulsions had been controlled by drugs. He had seen two or three at the Royal Alexandra Hospital for Children, mainly temporal lobe epileptics, who had been fairly free from behaviour problems until they were given "Mysoline". Their epileptic manifestations then subsided, and they began to exhibit serious behaviour disorders. Dr. Williams said that he had been interested in Dr. Nuffield's remarks about the activity of social workers at the Maudsley Hospital. He agreed with Dr. Hamilton that if the parents could have the actual mechanism of epilepsy in their child explained to them, the type of reasoning that he had experienced in Newcastle would be avoided: "I don't think we have to worry about it, Doctor; if I wet a towel and slap him on the face with it, he comes out of it." The next step was to believe that it was unnecessary to carry on with drug therapy under those conditions. If the parent had the situation explained to him, provided he had adequate intelligence, that type of thing would not be likely to happen.

Dr. Nuffield, in reply to Dr. Williams's question about temporal lobe attacks producing or aggravating behaviour disorders, said that he had encountered a few cases. He could not say what the mechanism was. It seemed as if the ictal attack itself was a sort of relief, and if that was denied to the organism, the devil must out in some way.

DR. D. C. MADDISON referred to the question of informing the parents about the meaning of the epileptic seizure. He thought it should be reemphasized, but from a different angle. It had been said that an epileptic child might be over-protected or rejected by its parents. There was clearly some dynamic reason for that. Dr. Maddison thought that to the list given by Dr. Nuffield of the various ways in which the parent should be approached by a social worker or by the doctor should be added some consideration of what the epileptic phenomenon meant to the parent in terms of the parent's own personality. A general statement could be made that a superficial approach to the problem would not go the whole way towards making normal the parents' attitude towards the child, because they tended to see the phenomenon of epilepsy or any other severe disturbance in childhood as in some way reflecting upon their own capacity as parents. That might involve them at a very deep level. In other words, the very fact of having an epileptic child might lead to a great deal of guilt and anxiety, which could often be relieved by adequate talking out with some type of professional person. In epilepsy in childhood, the surface manifestations must be explored, in order to understand what their deeper meaning might be. Dr. Maddison was certain that many parents carried an unnecessary load of guilt, which could be relieved by comparatively simple professional handling.

DR. J. A. C. BRASSIL offered a suggestion on the matter of the child whose seizures were controlled and who then presented a behaviour problem. He said that such a situation had to be considered in relation to the type of seizure and to the type of parental attitude. As Dr. Nuffield had emphasized, the attitude of the parent was often one of over-protection. When the seizures were no longer part of the picture of family life, then the cause of the over-protection was withdrawn. Dr. Brassil believed that behaviour problems were likely to occur under those circumstances, since the behaviour disorder was a reaction to the withdrawal of the over-protection.

Dr. Nuffield, in reply, said that he quite agreed with all Dr. Maddison's statements. As he had pointed out before, about 50% of parents with epileptic children presenting behaviour disorders did not respond to the superficial approach; something more had to be done. The child's epilepsy simply served as a focus for the psychopathological conditions to act on. The management of those

parents and those families was extremely difficult. At the Maudsley Hospital there were epileptic children who had been attending there for years, and whose parents had been worked on for a number of years—they presented very tough problems.

VICTORIAN BRANCH.

Section of Industrial Medicine.

THE next meeting of the Section of Industrial Medicine of the Victorian Branch of the British Medical Association will be held on Friday, October 4, 1957, at 8 p.m., in the lecture theatre of the Victorian Eye and Ear Hospital. It will take the form of a combined meeting with the Section of Otolaryngology. Dr. Hugh A. Kuhn, a visitor from the U.S.A., will present a paper on "Acoustic Trauma". This will be accompanied by a sound film, a tape recording and slides. All members of the British Medical Association will be welcome.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

DISCOURTEOUS TREATMENT OF MEDICAL EXAMINERS OF THE UNIVERSITY OF MELBOURNE.

[From the *Australasian Medical Gazette*, January, 1886.]

AT an adjourned meeting of the Melbourne University Council held on September 28 a letter was read from Dr. Rowan wherein he complained that he had not received a notice that it would be necessary to make a new application for the position of coexaminer in obstetric medicine which he held last year and that the appointment had been filled for the year before he knew that it was vacant. The Registrar explained that many of the old examiners did not send in applications and that notices were then sent to them. It was the duty of the Faculty of Medicine to see to the matter but they would not send notices to Dr. Rowan and Dr. Balls-Headley because they did not consider that these gentlemen should be appointed on account of their supposed hostile attitude to Dr. Jamieson the lecturer on obstetric medicine. The members of the council generally considered that the Faculty had acted in a very improper manner in forwarding notices to some former examiners and not to others. It was agreed to reply to Dr. Rowan's letter, expressing the regret of the council that he had not received notice of the necessity to make application for his reappointment and stating that the council fully recognized his past services.

We do not think it necessary to make any further remarks upon the conduct of the Registrar except to say that he seems to have been a very facile tool in the hands of the Faculty of Medicine in a matter which must cause a feeling of shame to arise in the members of our profession that their body should contain men capable of being guilty of such petty and contemptible conduct towards their professional confrères. If the governing body can act in such a manner it is hardly to be wondered at that the conduct of many of the students is such as to often call down upon them the condemnation of the public and the press of Victoria.

Correspondence.

PSYCHIATRIC CONSEQUENCES OF RAUWOLFIA THERAPY.

SIR: It is with dismay that one sees a scientific publication such as THE MEDICAL JOURNAL OF AUSTRALIA publish an article such as "Psychiatric Consequences of Rauwolfia Therapy", by F. J. Kyneur. Not surprisingly the lay Press seized avidly on this material and splashed it across its headlines; as a result many patients taking reserpine and similar drugs under proper medical supervision have been caused unnecessary alarm. It would be churlish to blame Dr. Kyneur for the excesses of the lay Press, but I have a quarrel to pick with him, not so much over the matter of his argument (which, I think, he weakens by overstating it), but the manner of its presentation which is replete with such colloquialisms as "wretched mental state" and "has intensely wretched ideas". There are no figures (except the meaningless total of 32 cases diagnosed by the author and his colleague in 18 months), no statistics, no references to other work in this field, no mention even of any other published clinical observation. One must conclude from all this that the author is living in some ivory tower into which no extraneous noise has so far penetrated.

Furthermore I should like to point out that in this brief article of some 1500 words the term "insanity" occurs no less than five times—this at a time when responsible bodies are attempting to remove this and similar offensive and out-dated terms from our present legislation. I would respectfully submit, Sir, that the most suitable place in your journal for "Psychiatric Consequences of Rauwolfia Therapy" is the "Out of the Past" column.

Yours, etc.,

E. J. A. NUFFIELD.

Royal Prince Alfred Hospital Medical Centre,
Carillon Avenue,
Newtown, N.S.W.
August 26, 1957.

PUBLIC HOSPITALS AND RADIOLOGICAL PRACTICE.

SIR: This Branch of The College of Radiologists of Australasia has long been concerned that there has been a slowly increasing tendency in this State for public hospitals to enter into the field of private radiological practice both in therapy and in diagnosis, the profession generally tending to regard the various public hospital X-ray departments as being available for the investigation or treatment of the private patient.

It is time that attention was once more drawn to the fact that these departments exist to take care of those patients who cannot afford private fees. The New South Wales Branch of the British Medical Association has in its circulars of October 15 and November 19 last year requested that medical practitioners should not refer patients able to pay to the X-ray departments of public hospitals, and it is the purpose of this communication to make known the terms of a resolution passed unanimously at the annual general meeting of the New South Wales Branch of the College on August 30 last. The resolution stated:

> That this Branch of the College of Radiologists of Australasia is of the opinion that private and intermediate patients (other than those occupying beds at the time) should not attend diagnostic or therapeutic X-ray departments of public hospitals when the services of a private radiological practice are available.

This Branch of the College seeks the support of the medical practitioners in New South Wales in adhering to this principle, which it regards as crucial to the long-term continuance of private radiological practice with the services it provides.

Yours, etc.,

BRIAN E. FRECKER,
Honorary Secretary, New South Wales Branch, The College of Radiologists of Australasia.

135 Macquarie Street,
Sydney,
September 4, 1957.

GUAIACOL-GLYCEROL-ETHER: A TRANQUILLIZING DRUG.[1]

SIR: Whilst we are sure that you do not wish your correspondence columns to become a debating ground for pharmaceutical houses, we feel that the letter from Mr. R. W. Easterbrook (August 10, 1957) does us an injustice.

[1] This correspondence is now closed.—EDITOR.

If Mr. Easterbrook will read our letter again, he will find that we make no comment, adverse or otherwise, on the use of guaiacol-glycerol-ether as a "tranquillizer". His statement that we belittle its use in this way is, therefore, quite unfounded.

Our letter was intended to provide useful information on the pharmacology of guaiacol-glycerol-ether, supplementing that contained in Dr. Vann's letter.

Yours, etc.,
THE CROOKES LABORATORIES LIMITED.

458-468 Wattle Street,
Ultimo,
Sydney.
September 4, 1957.

A SEVERE BASEBALL INJURY.

SIR: Reduction of dislocations of the interphalangeal joints is usually easily accomplished by applying traction to the finger and flexing it. The following case is interesting because, owing to the severity of the dislocation, reduction could not be performed except by operative means.

A man, aged 42 years, was struck on the tip of the right ring finger by the ball in a baseball match. The middle phalanx was dislocated backwards, and there was a deep transverse wound on the palmar surface of the finger just proximal to the joint. Attempts made to reduce the dislocation by traction failed. Open reduction was therefore carried out by making an incision on the dorsum of the finger. The joint cavity was found to be filled with blood clot. After removal of this, the bone was easily replaced. Five weeks later an X-ray film showed almost complete obliteration of the joint space. There is about 50% limitation of movement of the joint.

This severe type of baseball injury must be fairly common, but I can find little about it in text-books.

Yours, etc.,
S. U. HUMPHRIES, M.R.C.S., L.R.C.P.

Tennant Creek Hospital,
Tennant Creek,
Northern Territory.
August 23, 1957.

Hospitals.

ST. VINCENT'S HOSPITAL, SYDNEY.

THE St. Vincent's Hospital Society announces the Guest Professorship of Sir Russell Brock, M.S., F.R.C.S., Surgeon to Guy's Hospital, London, and the Brompton Hospital for Chest Diseases, from September 16 to October 2, 1957, and also the St. Vincent's Hospital Society Reunion Week from September 30 to October 5, 1957. The lectures and the operative and clinical sessions are open to any members of the medical profession who are interested in attending. The Honorary Secretary of the St. Vincent's Hospital Society is Dr. W. J. Burke, 185 Macquarie Street, Sydney.

Guest Professorship of Sir Russell Brock.

There will be morning and afternoon sessions, on the dates to be shown. The morning sessions will consist of operations, which will be viewed in the television room from 9 a.m. In the afternoons clinical sessions, beginning at 2.30 p.m., will be held in the new lecture theatre. The programme is as follows: Monday, September 23: morning, operation; afternoon, "Pulmonary Stenosis", Dr. R. Jeremy. Tuesday, September 24: morning, operation; afternoon, "Coarctation and Aortic Aneurysm", Mr. P. J. Heery. Wednesday, September 25: morning, operation. Thursday, September 26: morning, operation; afternoon, "Ventricular Septal Defect", Dr. A. Seldon. Monday, September 30: morning, operation; afternoon, "Unusual Cardiac Conditions", Mr. H. M. Windsor.

St. Vincent's Hospital Society Reunion Week.

The programme is as follows: Tuesday, October 1: 2 p.m., Guest Lecture, "Basic Principles in the Diagnosis of Chest Disease", Sir Russell Brock; 3.45 p.m., "Moles" (a symposium), Mr. J. P. Fleming, Dr. J. Garvan, Mr. L. Atkinson; 4.30 p.m., "The Modern Treatment of Burns", Mr. N. C. Newton. Wednesday, October 2: Guest Lecture, "Chest Injuries", Sir Russell Brock (Stawell Hall, The Royal Australasian College of Physicians). Thursday, October 3: morning, clinics—neurology and neurosurgery, and gastroenterology; 2 p.m., "The Modern Treatment of Thyro-

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED AUGUST 31, 1957.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	6(4)	2(2)	1	..	..	..	..	9
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	1(1)	..	..	..	..	..	1
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	1	..	..	..	1	..	..	..	2
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	4(4)	3(1)	..	..	..	..	..	7
Diphtheria	2(1)	..	1(1)	1	1(1)	..	..	..	5
Dysentery (Bacillary)	..	..	1(1)	1(1)	1(1)	..	..	..	3
Encephalitis	..	..	..	..	1(1)	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	1	1
Infective Hepatitis	44(21)	7	2(1)	9(4)	23(5)	1(1)	1	..	87
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	45(1)	..	..	..	..	..	45
Malaria	..	..	..	..	..	..	2	..	2
Meningococcal Infection	2(1)	4(3)	3(2)	..	..	4	..	..	13
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	1(1)	1(1)	..	..	1(1)	..	..	2
Puerperal Fever	..	..	..	..	..	..	..	..	2
Rubella	..	24(13)	1	34(11)	10(10)	..	..	..	69
Salmonella Infection	..	..	..	1(1)	..	..	..	..	1
Scarlet Fever	11(7)	6(4)	7(4)	6(3)	1(1)	..	1	..	32
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	2(2)	..	..	..	..	..	..	2
Trachoma	..	..	..	..	7	..	1	..	8
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	15(9)	24(22)	7(1)	2	2(2)	5(4)	3	..	58
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

toxicosis", Dr. Bryan Curtin; 2.30 p.m., "Aortic Stenosis at St. Vincent's", Dr. George Hall; 3.45 p.m., "The Acute Gall-Bladder at St. Vincent's", Mr. P. J. Kenny; 4.30 p.m., "Hæmorrhage in Obstetrics", Mr. R. J. F. McInerney; 8.15 p.m., "The Meaning of Headache", Sir Geoffrey Jefferson, O.B.E., F.R.S., Emeritus Professor of Neurosurgery in the University of Manchester. Friday, October 4: morning, clinics (chest clinic); 2 p.m., Guest Lecture, "Post-Operative Chest Complications", Sir Russell Brock; 3.45 p.m., "Abdominal Pain in Childhood", Mr. David Dey; 4.30 p.m., "Should the Tonsils Come Out?"; 8 p.m., "Inside China", Mr. Douglas Miller.

The College of Radiologists of Australasia.

ANNUAL MEETING.

THE annual meeting of The College of Radiologists of Australasia will be held in Perth from October 20 to 25, 1957. Particulars may be obtained from Dr. D. E. Copping, Publicity Officer, 29 Adelaide Street, Fremantle.

Notice.

INTERNATIONAL CHILDREN'S CENTRE.

THE following information relates to the activities of the International Children's Centre, Paris.

Guigoz Scholarship in Nutrition.

The Guigoz Scholarship in Nutrition for the year 1958-1959 will be awarded by the International Children's Centre. The closing date for applications is May 15, 1958. Applicants should send the following details: (i) a *curriculum vitæ*, setting out their studies on biological and social problems pertaining to nutrition or to infant and child feeding; (ii) a letter of recommendation from one of their masters; (iii) a statement on the studies they wish to pursue with the aid of the Guigoz Scholarship. Applicants must have an adequate knowledge of the French language. At the conclusion of the scholarship period, scholars will be expected to send to the International Children's Centre a scientific paper on the subject which they have studied during the year. Applications should be sent to the International Children's Centre, Château de Longchamp, Bois de Boulogne, Paris XVI^{e}, France.

List of Courses Proposed for 1958.

At its session on June 30, 1957, the Executive Board of the International Children's Centre approved courses on the following subjects to be arranged by the Centre in 1958: day and residential nurseries, January 6 to 26; mentally defective children, January 27 to March 2; social pædiatrics (Dakar), February 24 to April 4; tuberculosis in the child (in French and in English), March 3 to 30; social pædiatrics, April 14 to July 6; nutrition, September 15 to October 12; maternal and child welfare for social and administrative personnel, October 13 to December 20; also a maternal and child welfare training course for African midwives (Dakar).

Royal Australasian College of Surgeons.

NEW SOUTH WALES MEETING.

A MEETING of the New South Wales Fellows of the Royal Australasian College of Surgeons will be held at Tamworth on Saturday and Sunday, October 26 and 27, 1957. The lectures and demonstrations will be held at the Tamworth Base Hospital. The programme is as follows:

Saturday, October 26: 2.30 p.m., "Immediate Management of Spinal Injuries", Mr. I. D. Miller; 4.15 p.m., "The Management of Urinary Tract Trauma", Mr. J. L. Watt and Mr. W. R. Lang.

Sunday, October 27: 10 a.m., selected surgical cases; 11.30 a.m., "Indications for Internal Fixation in Fractures of the Long Bones", Mr. F. H. McClements Callow.

A buffet dinner, at which wives and/or a guest will be welcome, will be held on Saturday, October 26. Accommodation in Tamworth should be booked before September 30, either through the State Secretary of the College at 139 Macquarie Street, Sydney (telephone BW 2083), or through Mr. J. L. Watt, 11 Fitzroy Street, Tamworth. At the same time it should be stated whether attendance at the dinner is desired.

All medical practitioners are invited to attend this meeting.

Deaths.

THE following death has been announced:

THWAITES.—Alexander Hopkins Thwaites, on September 9, 1957, at Balwyn, Victoria.

Diary for the Month.

SEPT. 24.—New South Wales Branch, B.M.A.: Ethics Committee.
SEPT. 25.—Victorian Branch, B.M.A.: Branch Council.
SEPT. 26.—New South Wales Branch, B.M.A.: Branch Meeting.
SEPT. 27.—Queensland Branch, B.M.A.: Council Meeting.
OCT. 1.—New South Wales Branch, B.M.A.: Council Quarterly.
OCT. 2.—Victorian Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, 88 L'Estrange Terrace, Kelvin Grove, Brisbane, W.1): All applicants for Queensland State Government Insurance Office positions are advised to communicate with the Honorary Secretary of the Branch before accepting posts.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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